Electronic supporting information for: Introducing *N*-, *P*-, and *S*-donor leaving groups: an investigation of the chemical and biological properties of monomeric thiopyridone piano-stool complexes

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Contents

NMR spectra

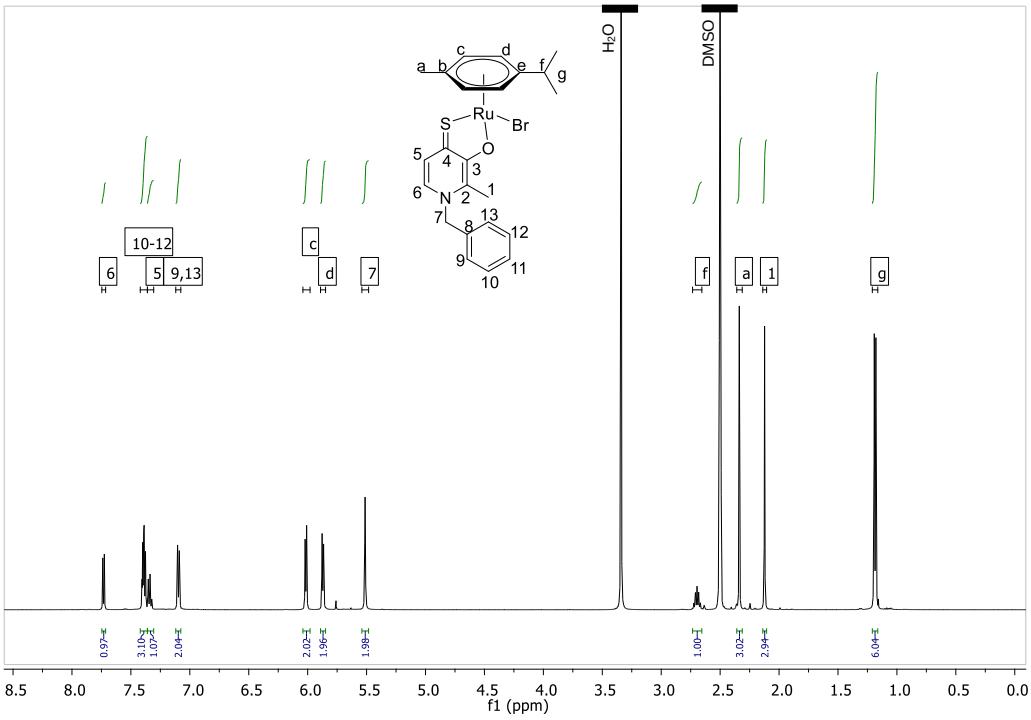

Fig. S1 ^{1}H-NMR of complex **H1** (500.10 MHz, d_6-DMSO, 25 °C).

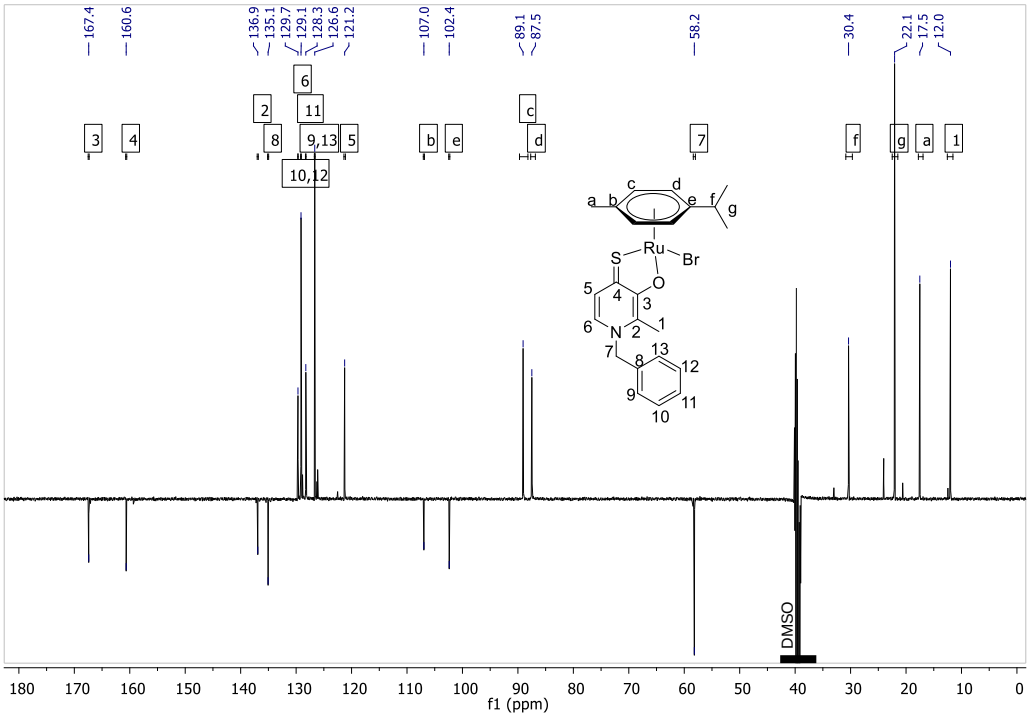

Fig. S2 ^{13}C-NMR of complex **H1** (125.75 MHz, d_6-DMSO, 25 °C).

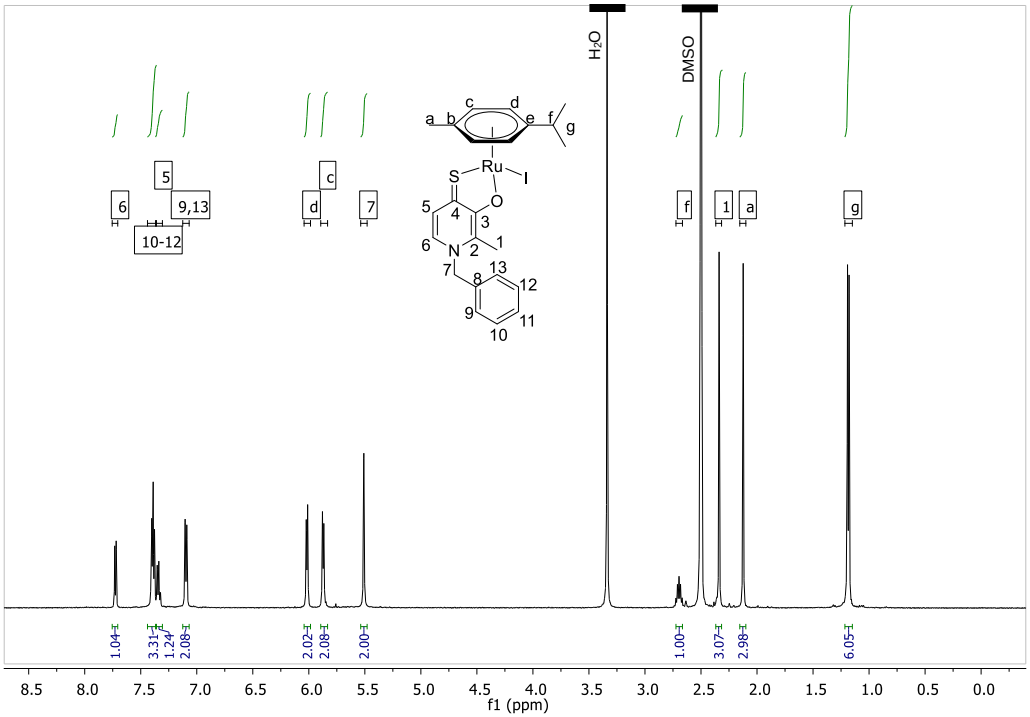

Fig. S3 ^{1}H-NMR of complex **H2** (500.10 MHz, d_6-DMSO, 25 °C).

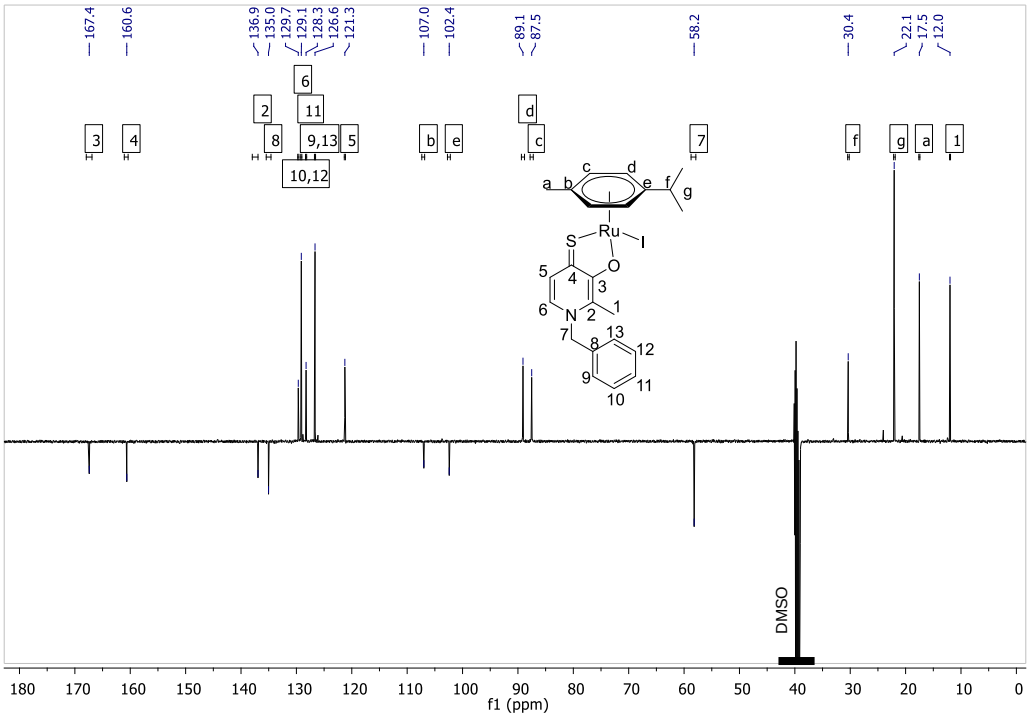

Fig. S4 ^{13}C-NMR of complex **H2** (125.75 MHz, d_6-DMSO, 25 °C).

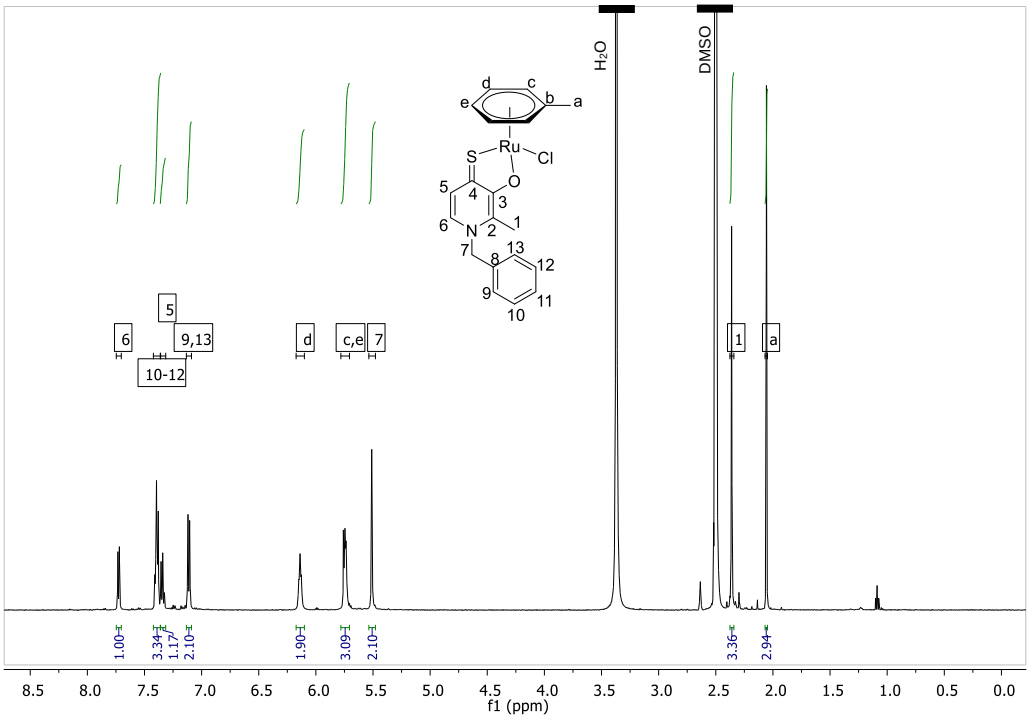

Fig. S5 ^{1}H-NMR of complex **H3** (500.10 MHz, d_6-DMSO, 25 °C).

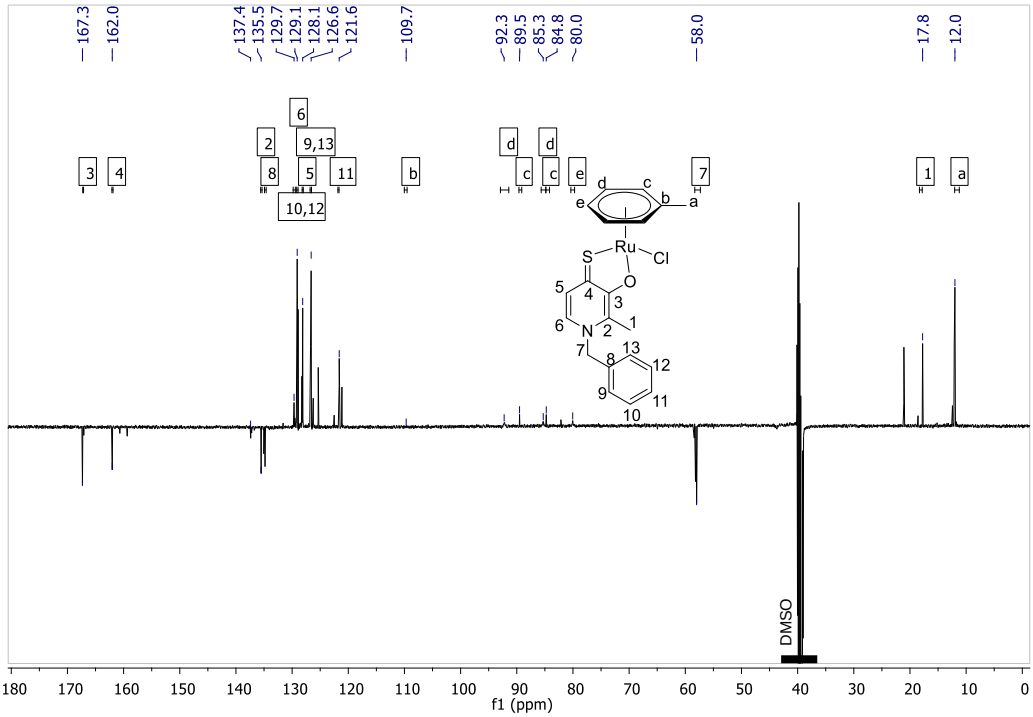

Fig. S6 ^{13}C-NMR of complex **H3** (125.75 MHz, d_6-DMSO, 25 °C).

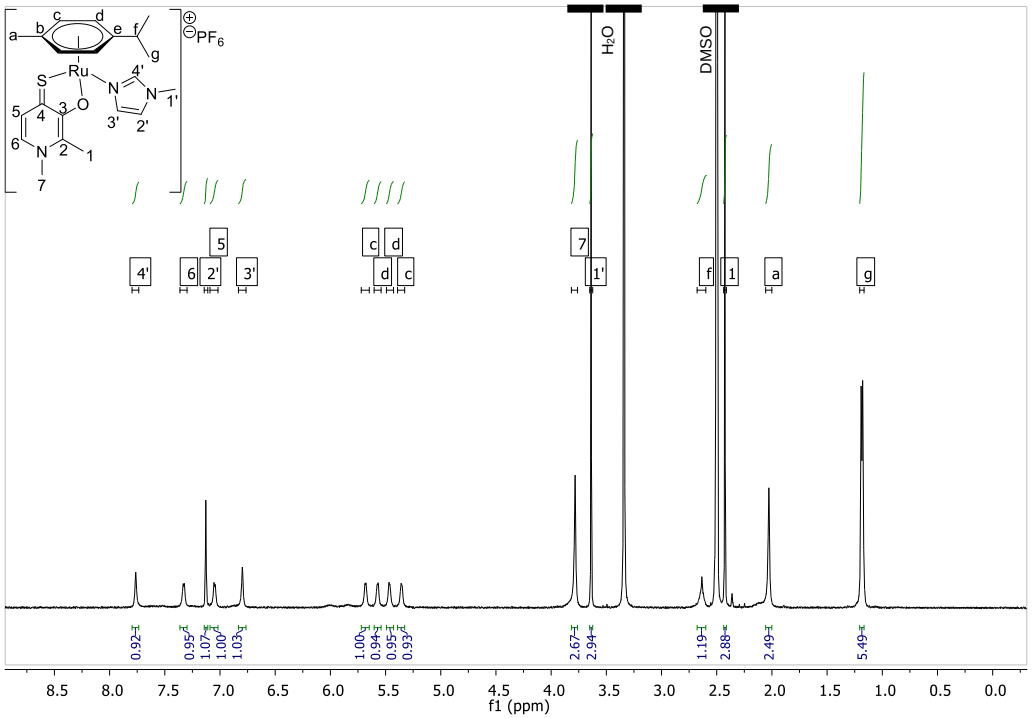

Fig. S7 ^{1}H-NMR of complex **N1** (500.10 MHz, d_6-DMSO, 25 °C).

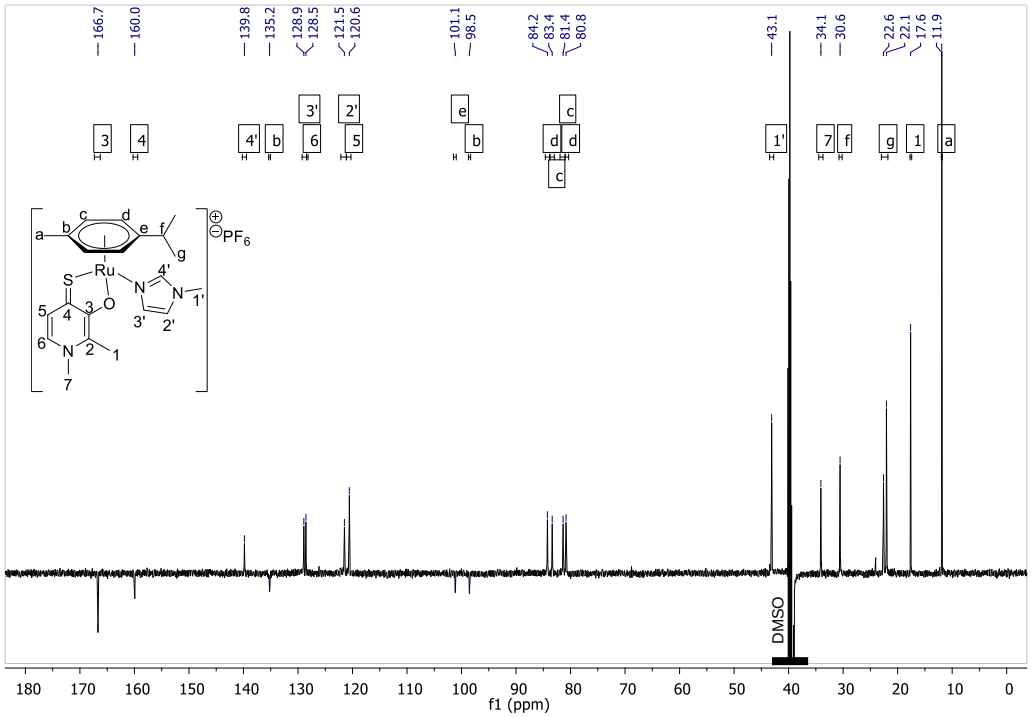

Fig. S8 ^{13}C-NMR of complex **N1** (125.75 MHz, d_6-DMSO, 25 °C).

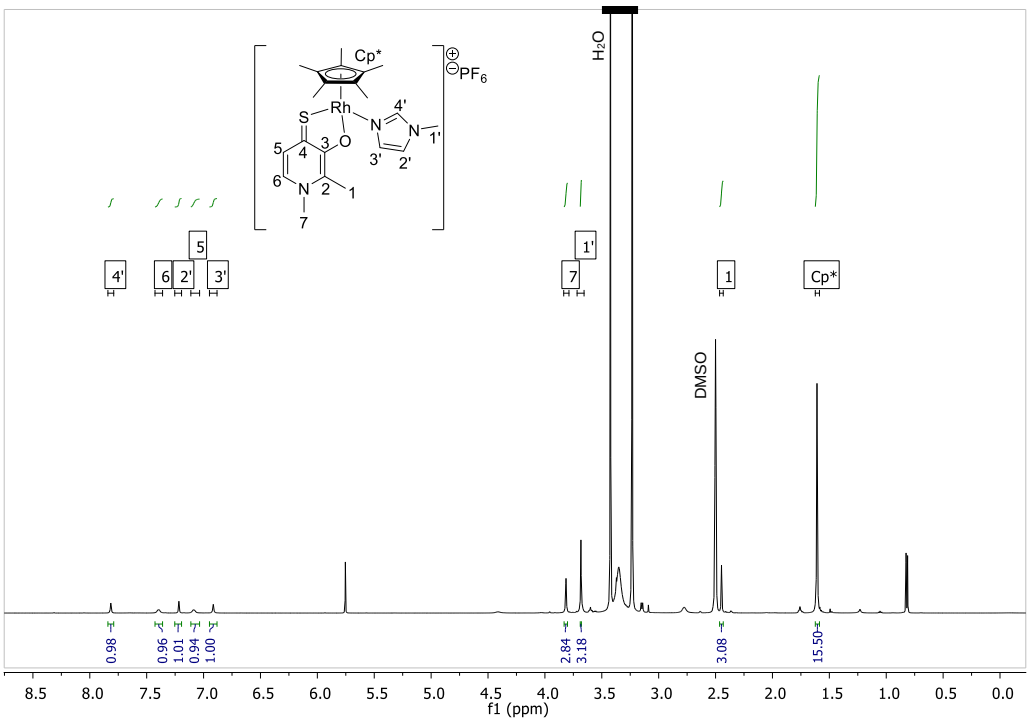

Fig. S9 ^{1}H-NMR of complex **N2** (500.10 MHz, d_6-DMSO, 25 °C).

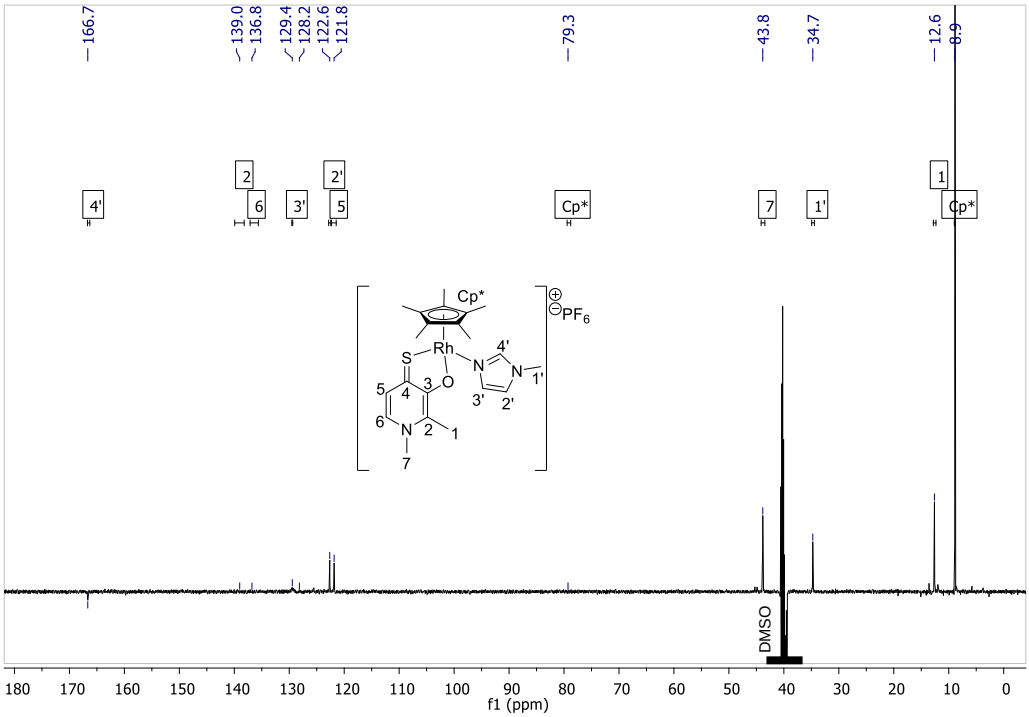

Fig. S10 ^{13}C-NMR of complex **N2** (125.75 MHz, d_6-DMSO, 25 °C).

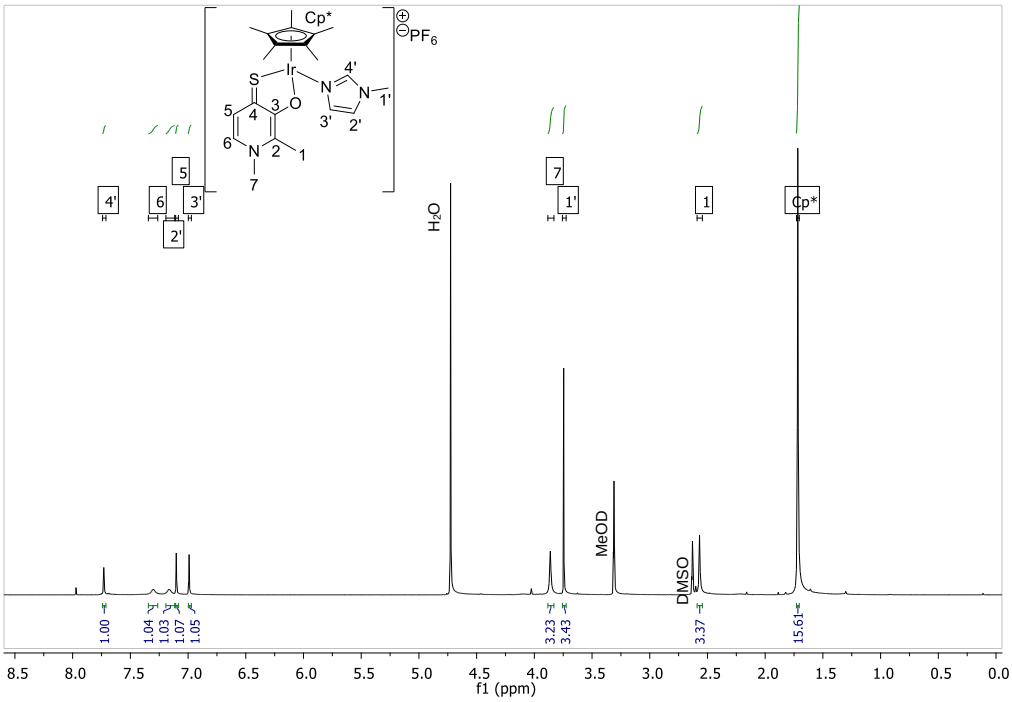

Fig. S11 ^{1}H-NMR of complex **N3** (600.25 MHz, d_4-MeOD, 25 °C); + 80 µL d_6-DMSO for better solubility.

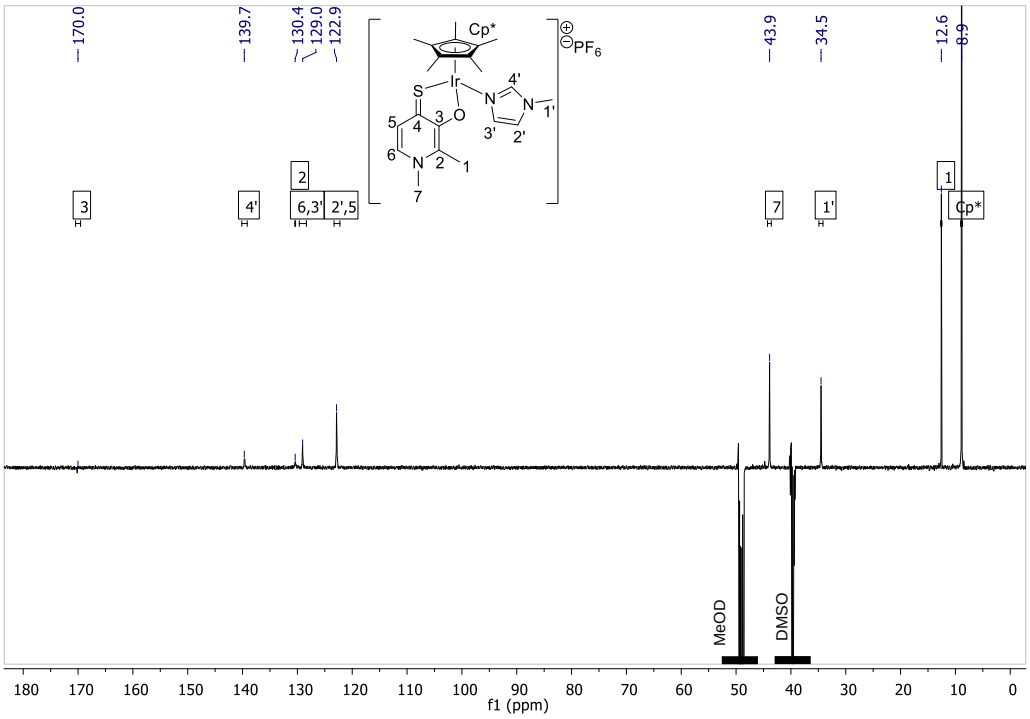

Fig. S12 ^{13}C-NMR of complex **N3** (150.95 MHz, d_4-MeOD, 25 °C); + 80 µL d_6-DMSO for better solubility.

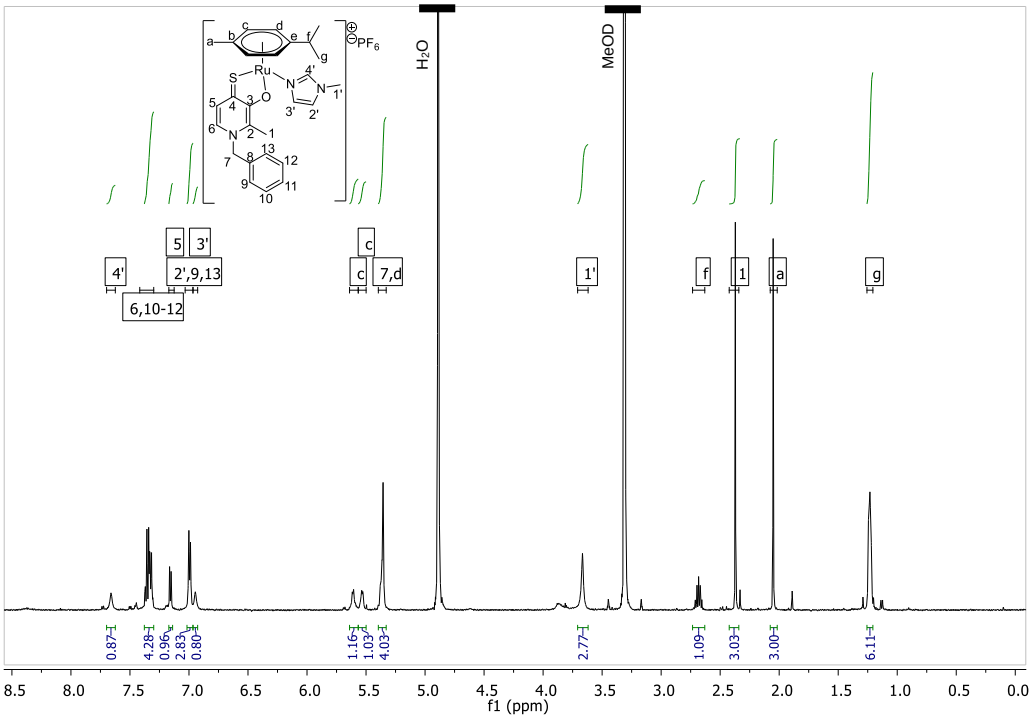

Fig. S13 ^{1}H-NMR of complex **N4** (500.21 MHz, d_4-MeOD, 25 °C).

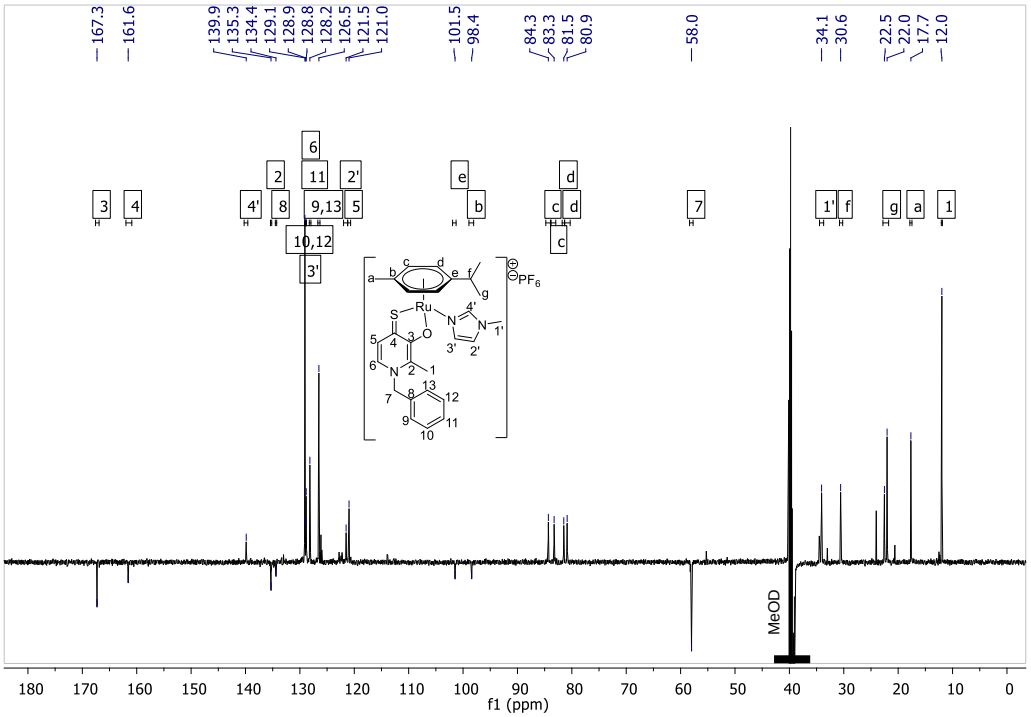

Fig. S14 ^{13}C-NMR of complex **N4** (125.75 MHz, d_4-MeOD, 25 °C).

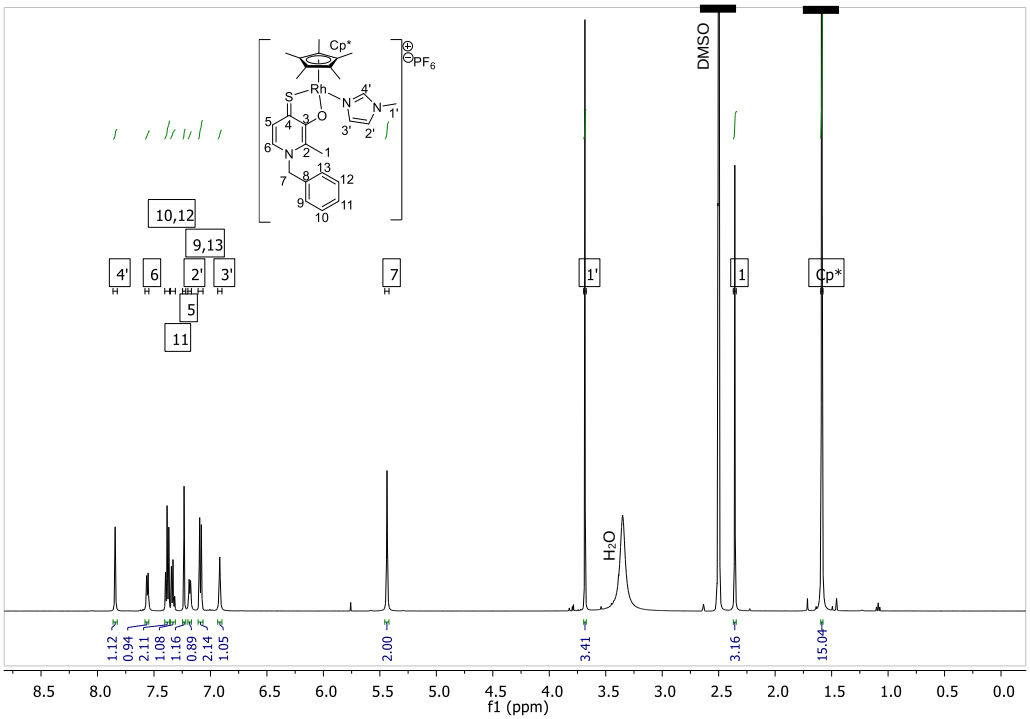

Fig. S15 ^{1}H-NMR of complex **N5** (500.32 MHz, d_6-DMSO, 25 °C).

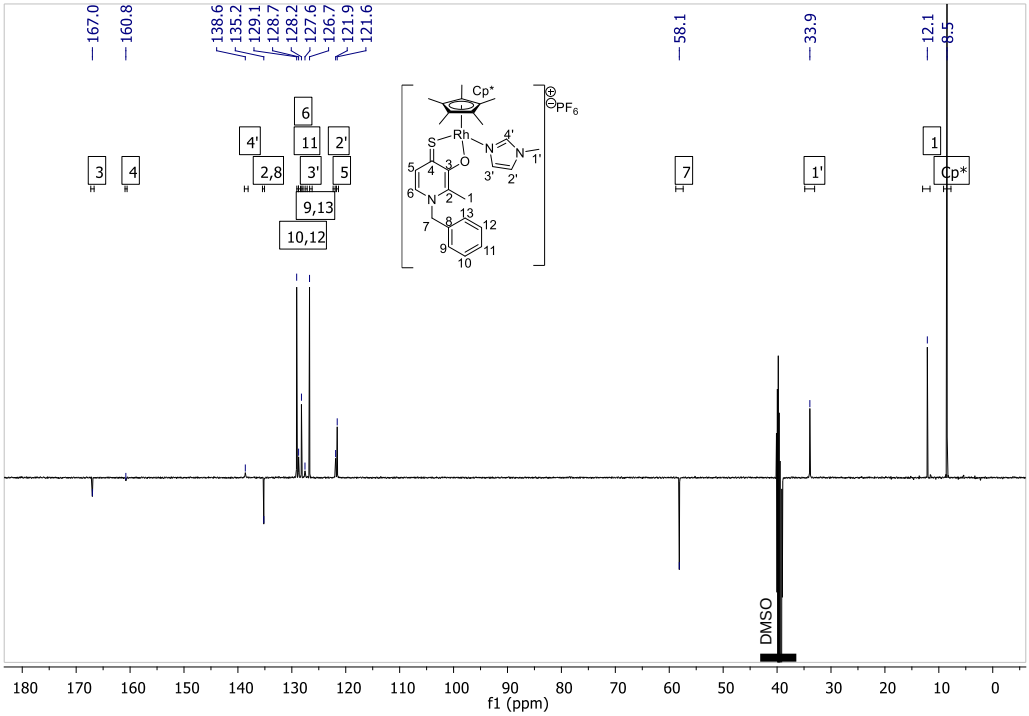

Fig. S16 ^{13}C-NMR of complex **N5** (125.81 MHz, d_6-DMSO, 25 °C)..

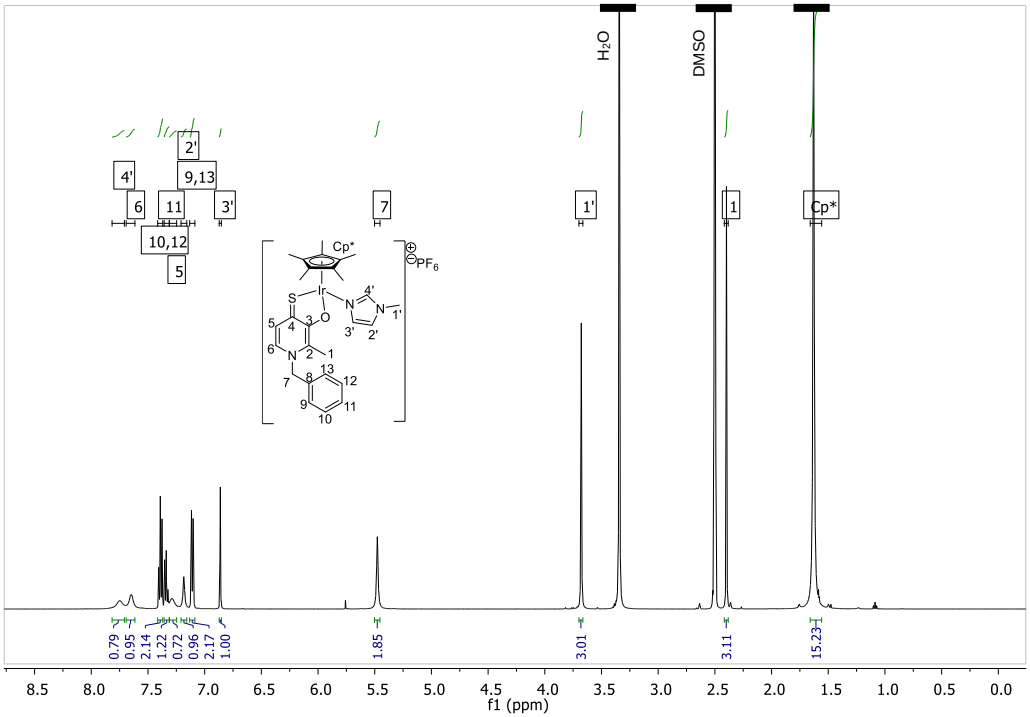

Fig. S17 ^{1}H-NMR of complex **N6** (500.32 MHz, d_6-DMSO, 25 °C).

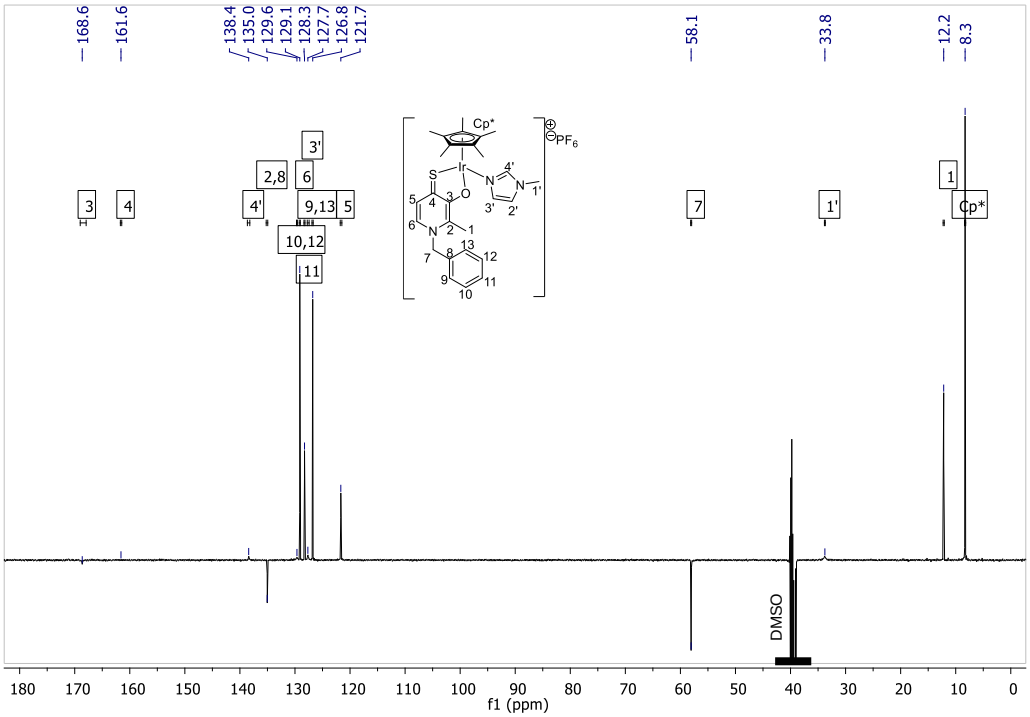

Fig. S18 ^{13}C-NMR of complex **N6** (125.81 MHz, d_6-DMSO, 25 °C).

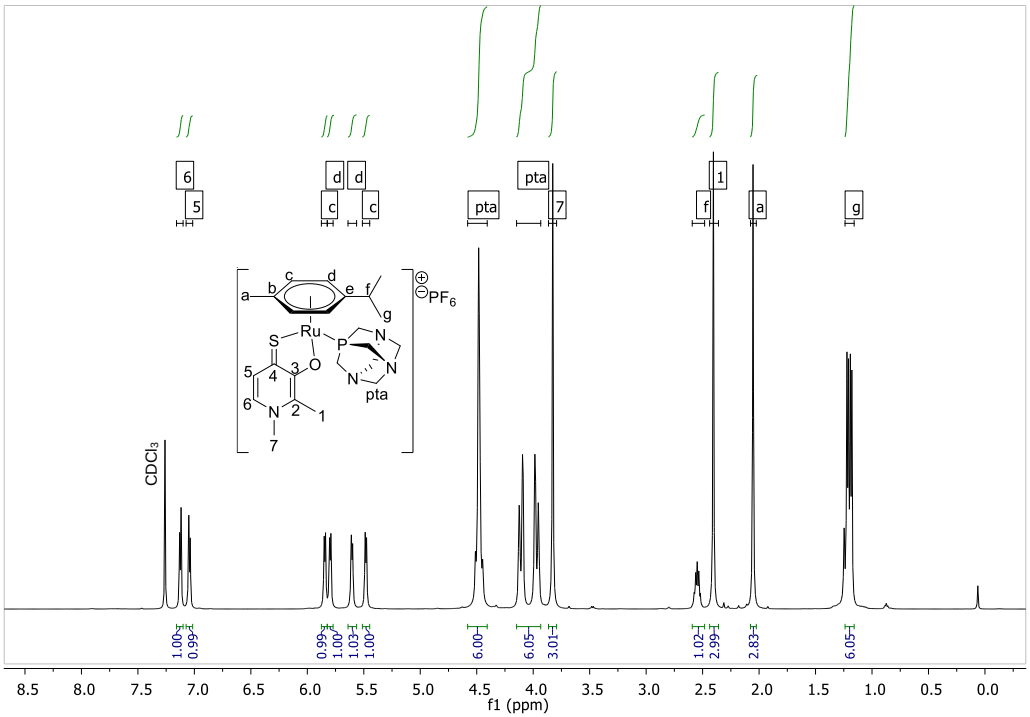

Fig. S19 ^{1}H-NMR of complex **P1** (500.32 MHz, $CDCl_3$, 25 °C).

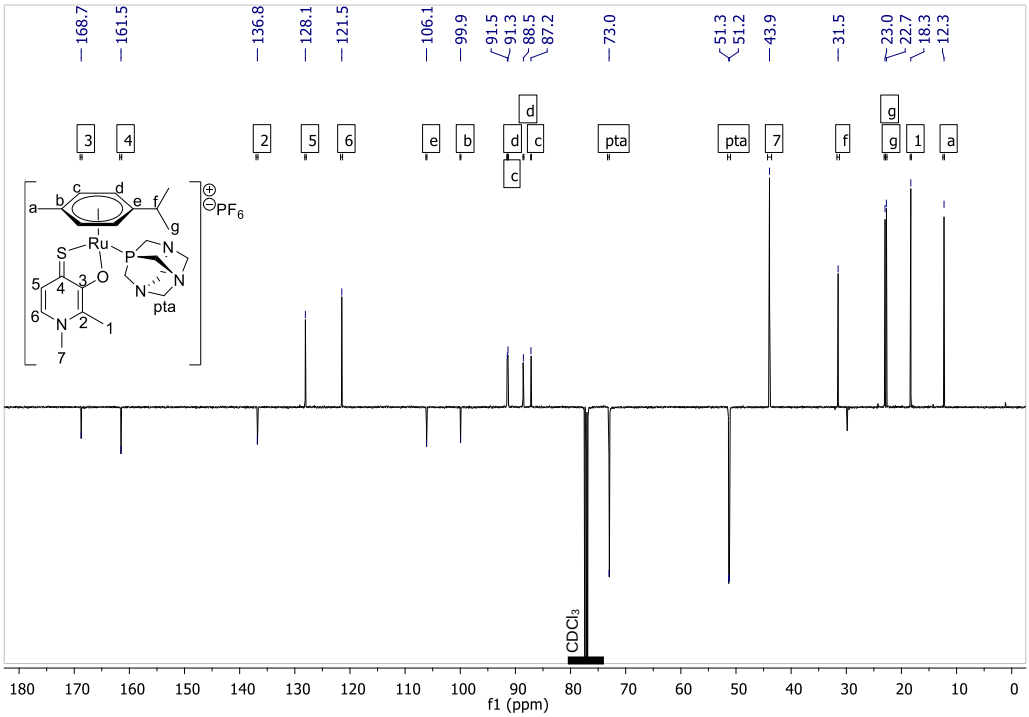

Fig. S20 ^{13}C-NMR of complex **P1** (125.81 MHz, $CDCl_3$, 25 °C).

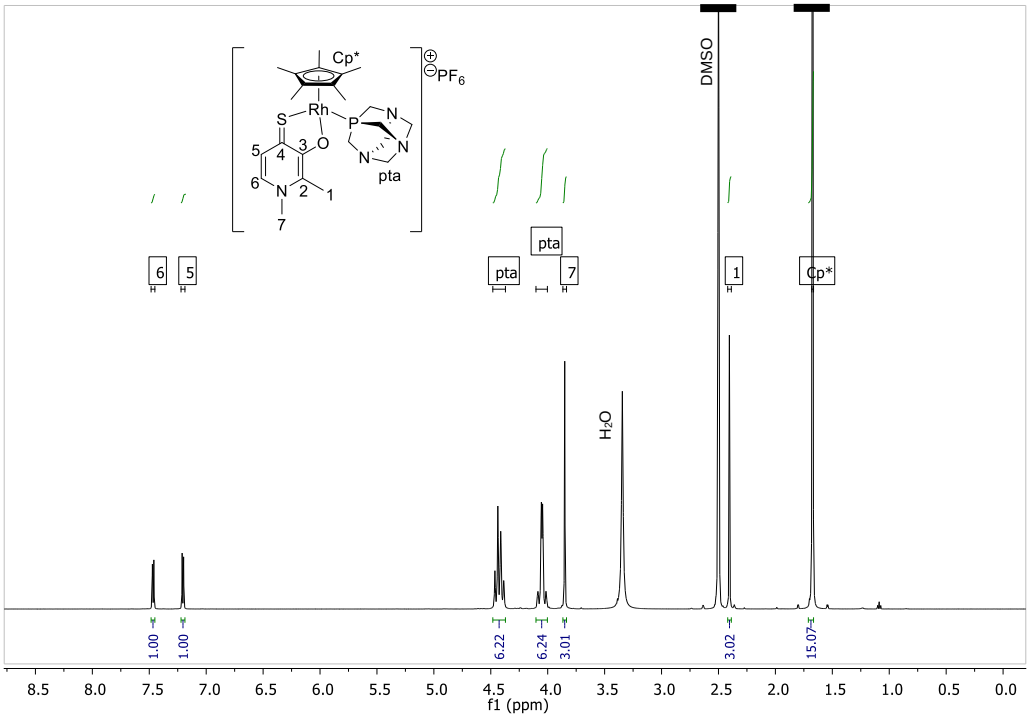

Fig. S21 ^{1}H-NMR of complex **P2** (500.32 MHz, d_6-DMSO, 25 °C).

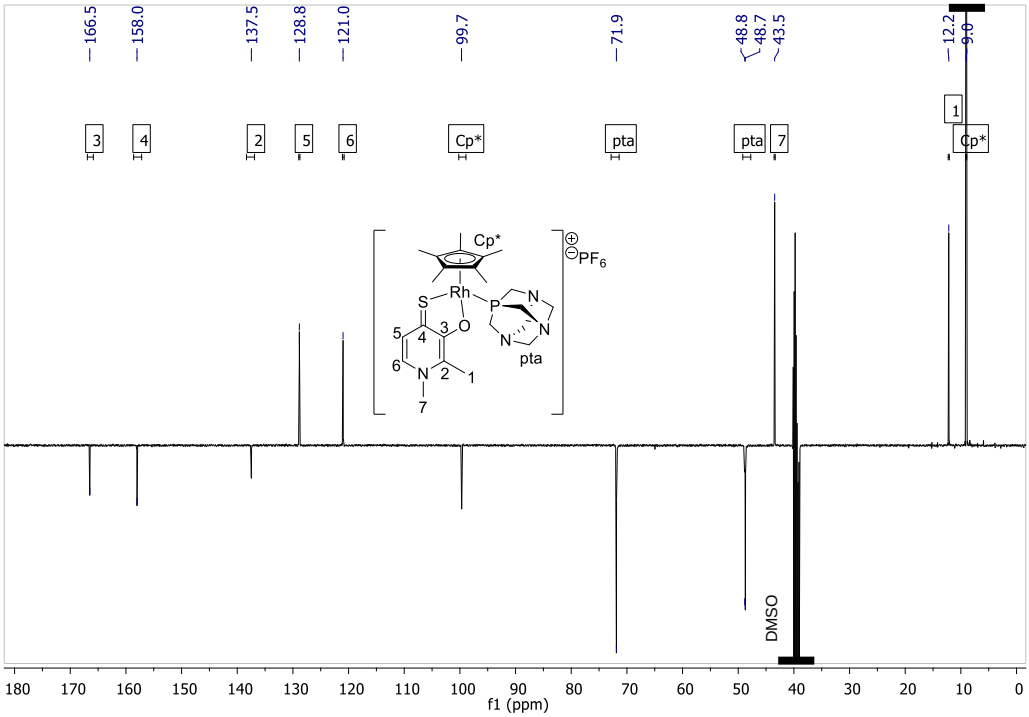

Fig. S22 ^{13}C-NMR of complex **P2** (125.81 MHz, d_6-DMSO, 25 °C).

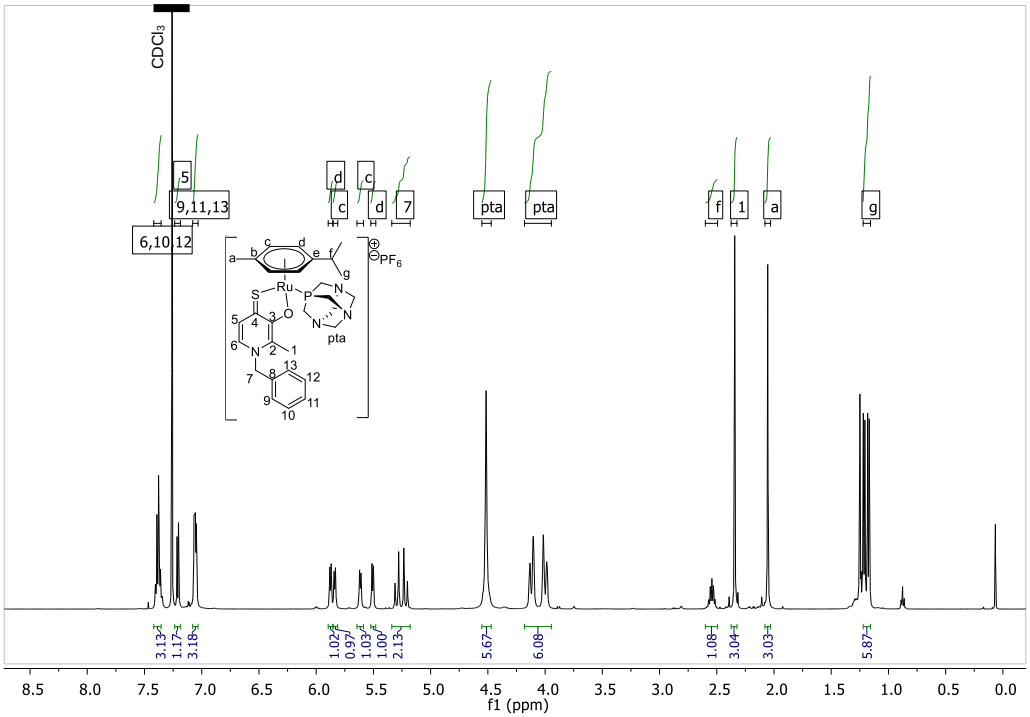

Fig. S23 ^{1}H-NMR of complex **P3** (500.32 MHz, $CDCl_3$, 25 °C).

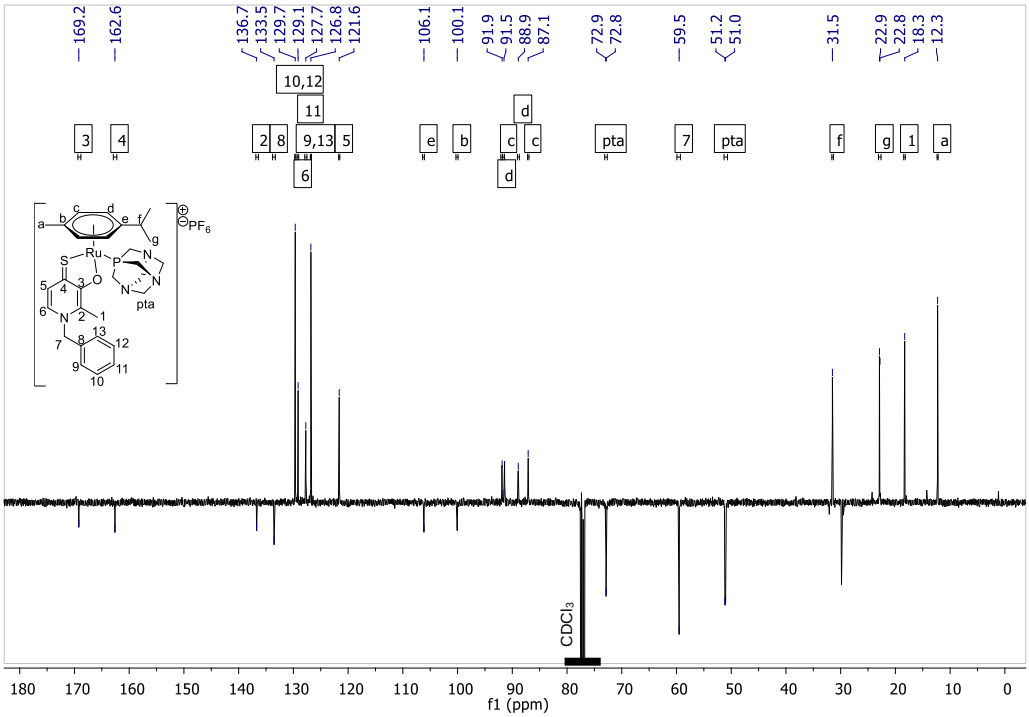

Fig. S24 ^{13}C-NMR of complex **P3** (125.81 MHz, $CDCl_3$, 25 °C).

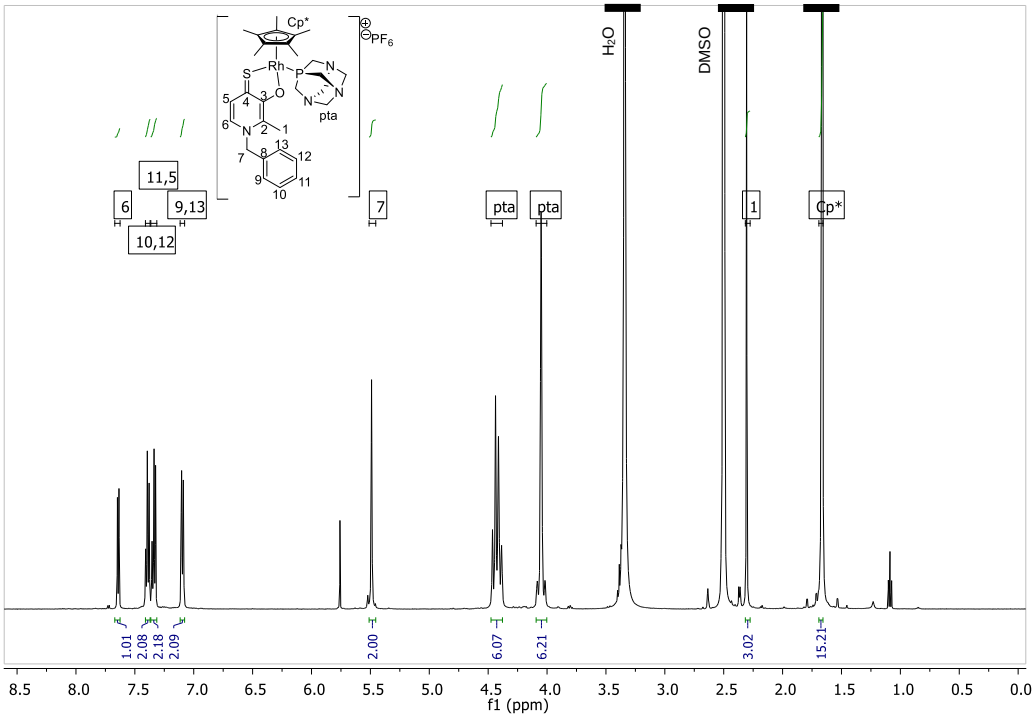

Fig. S25 ^{1}H-NMR of complex **P4** (500.32 MHz, d_6-DMSO, 25 °C).

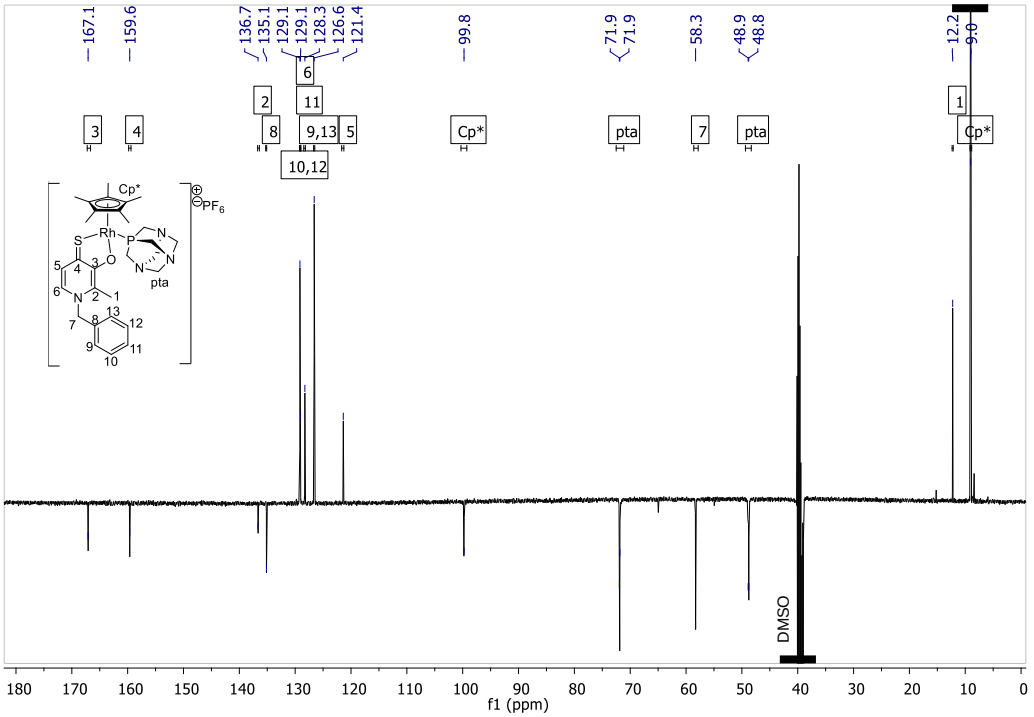

Fig. S26 ^{13}C-NMR of complex **P4** (125.81 MHz, d_6-DMSO, 25 °C).

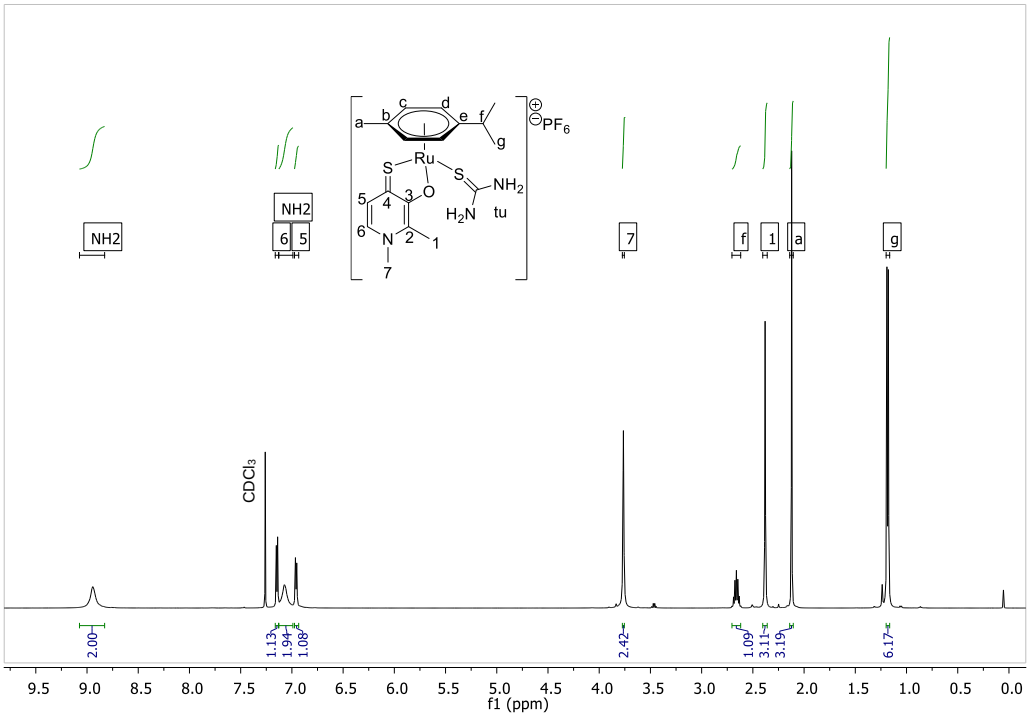

Fig. S27 ^{1}H-NMR of complex **S1** (500.32 MHz, $CDCl_3$, 25 °C).

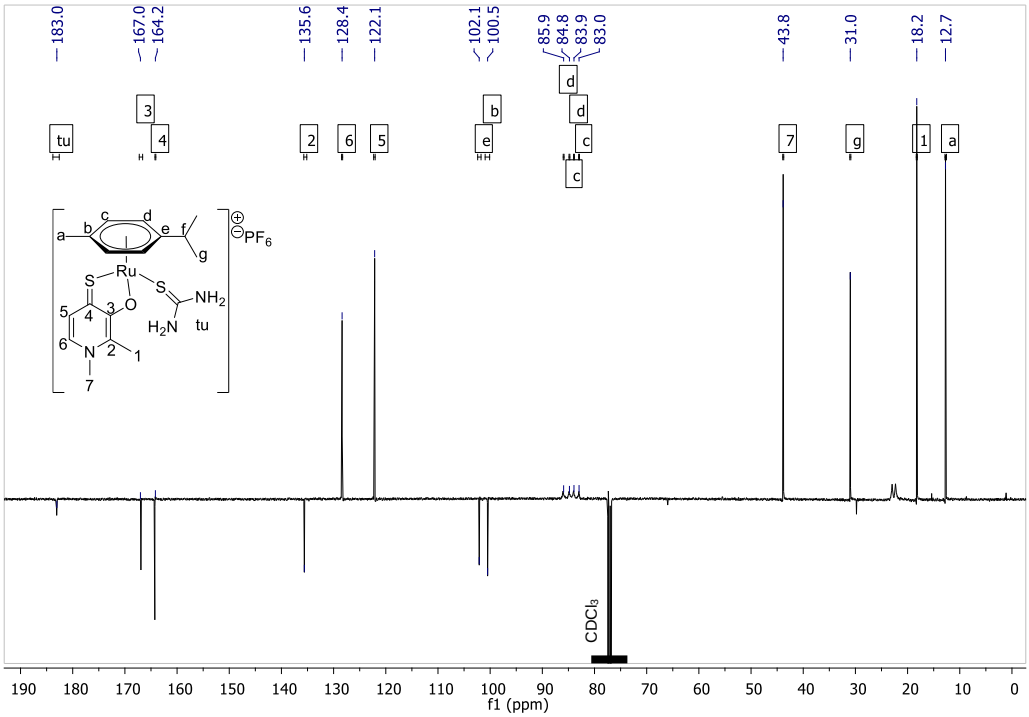

Fig. S28 ^{13}C-NMR of complex **S1** (125.81 MHz, $CDCl_3$, 25 °C).

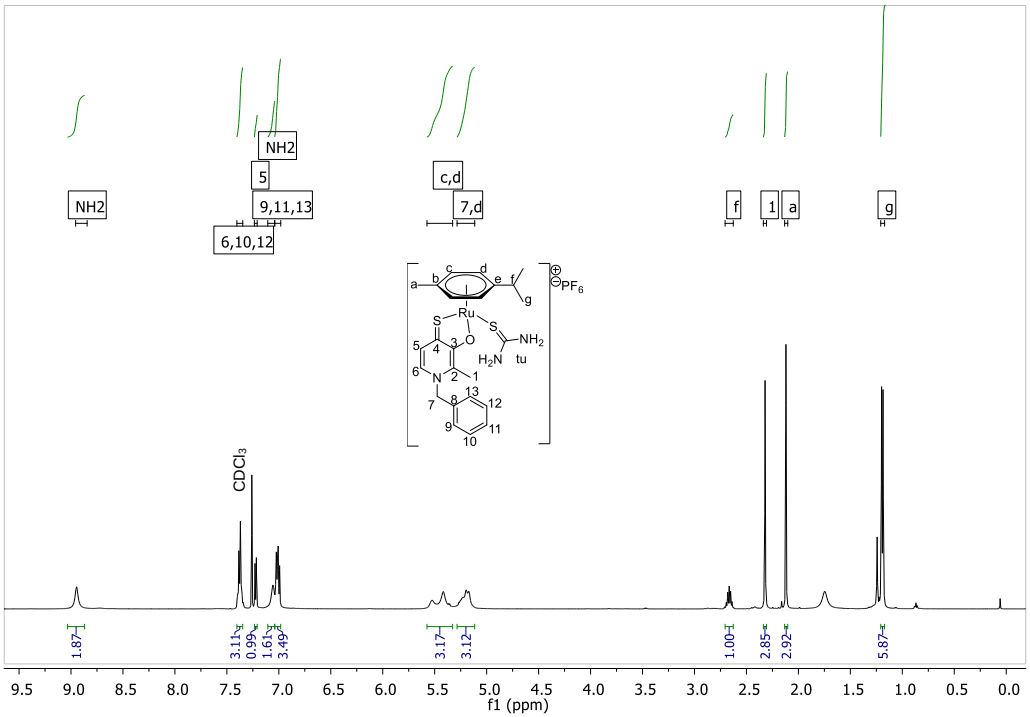

Fig. S29 ^{1}H-NMR of complex **S2** (500.32 MHz, $CDCl_3$, 25 °C).

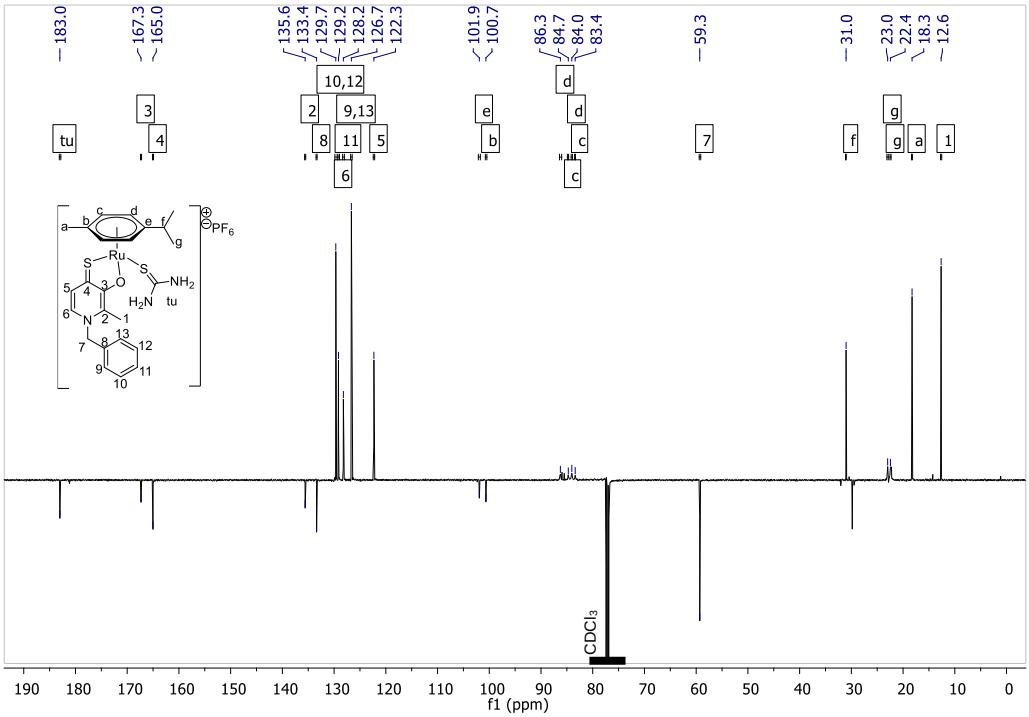

Fig. S30 ^{13}C-NMR of complex **S2** (125.81 MHz, $CDCl_3$, 25 °C).

NMR spectra in D_2O (Charges omitted for clarity)

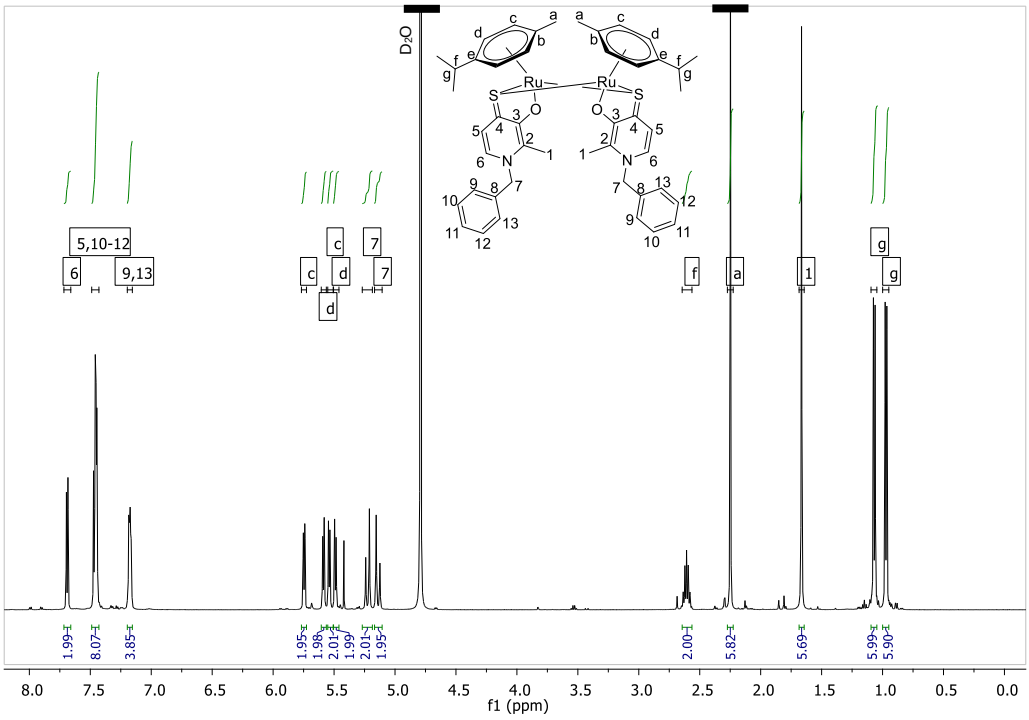

Fig. S31 ^{1}H-NMR of complex **H1*** (500.10 MHz, D_2O, 25 °C).

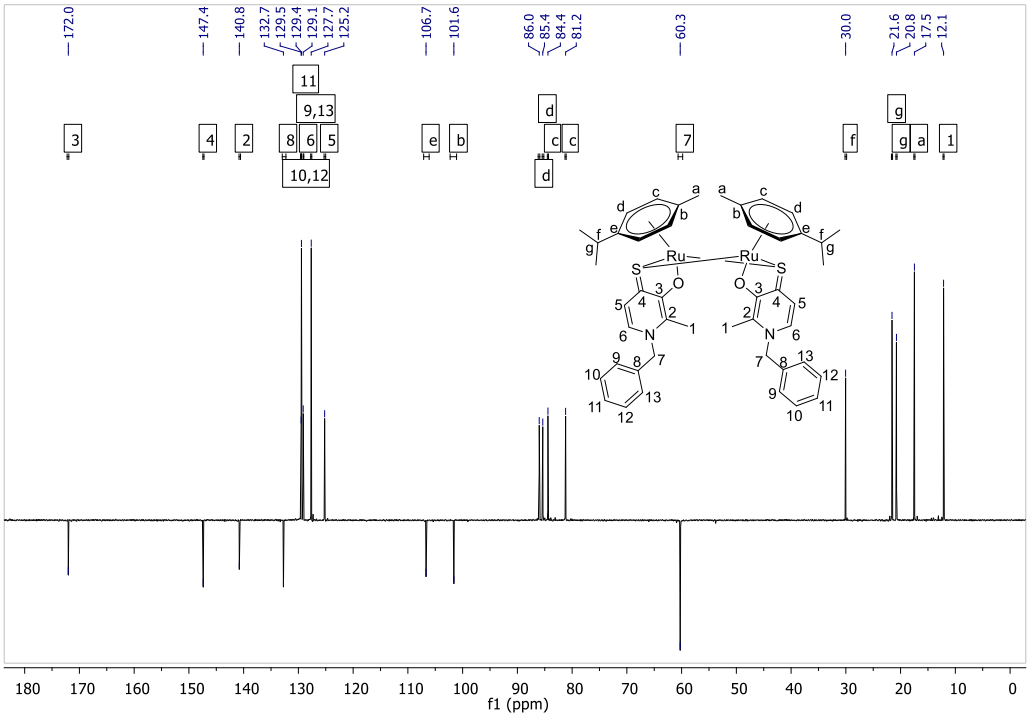

Fig. S32 ^{13}C-NMR of complex **H1*** (125.75 MHz, D_2O, 25 °C).

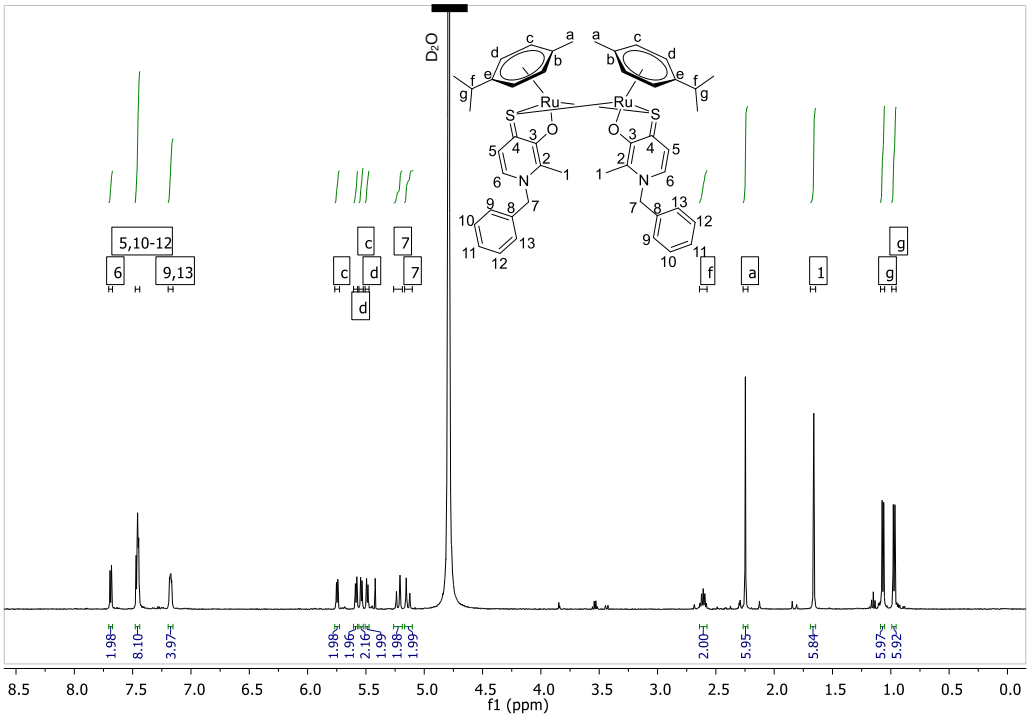

Fig. S33 ^{1}H-NMR of complex **H2*** (500.10 MHz, D_2O, 25 °C).

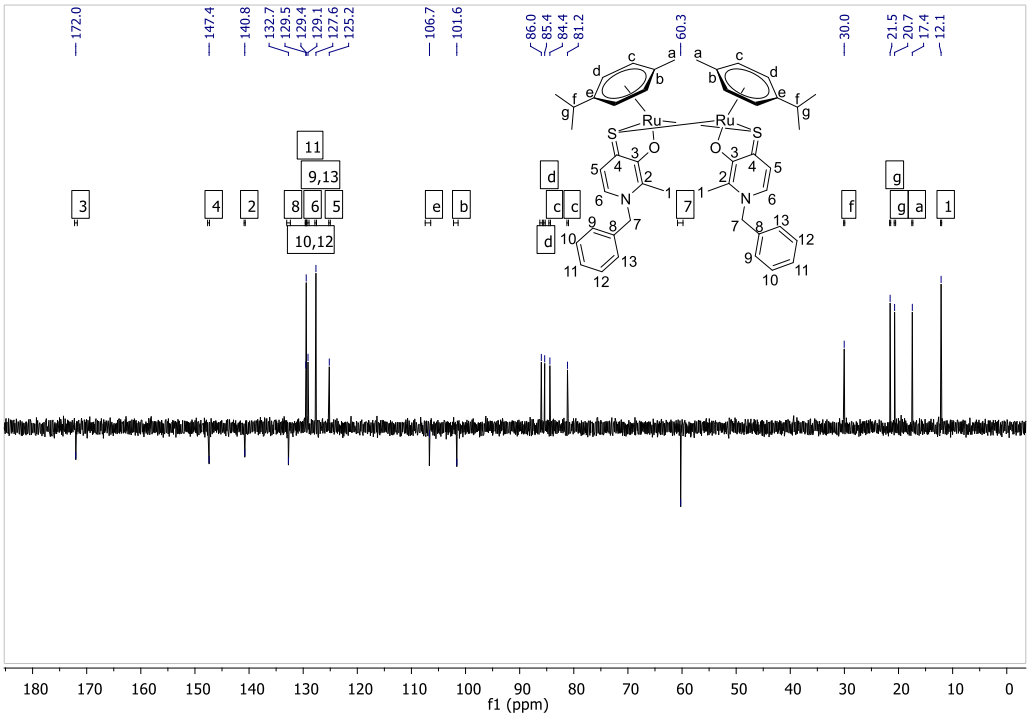

Fig. S34 ^{13}C-NMR of complex **H2*** (125.75 MHz, D_2O, 25 °C).

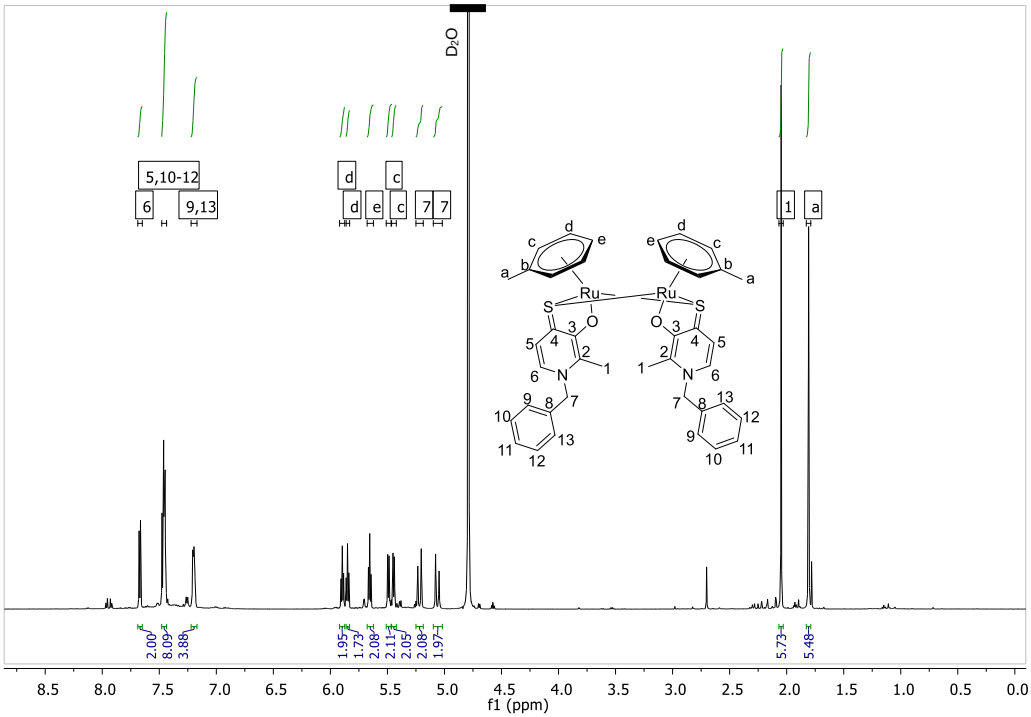

Fig. S35 ^{1}H-NMR of complex **H3*** (500.10 MHz, D_2O, 25 °C).

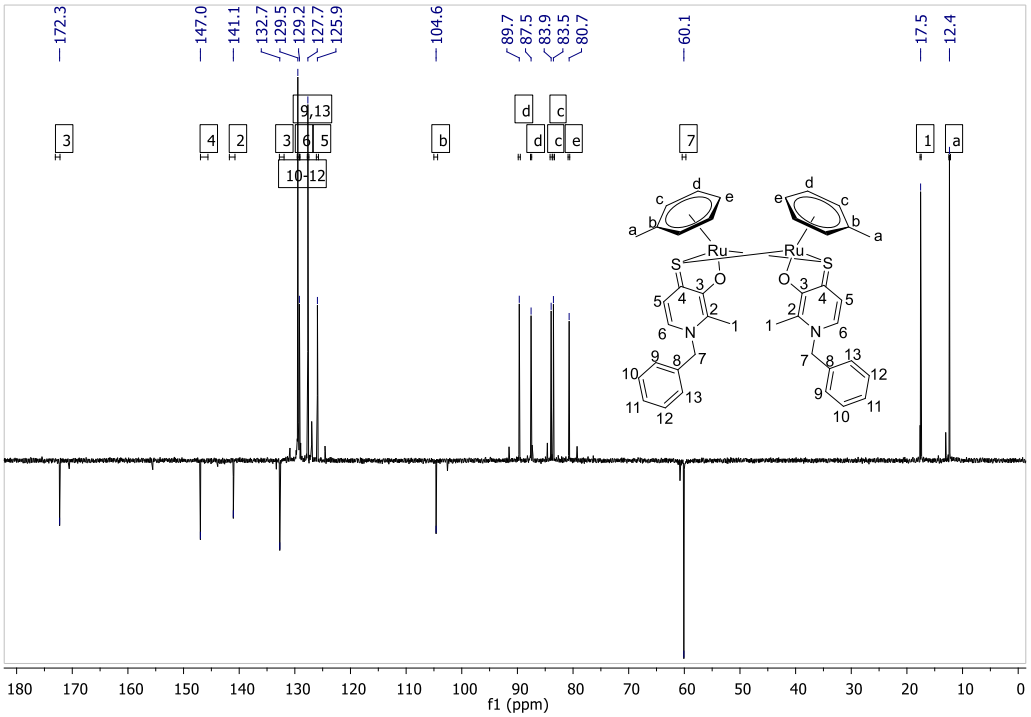

Fig. S36 ^{13}C-NMR of complex **H3*** (125.75 MHz, D_2O, 25 °C).

X-Ray data

Table S1 Experimental parameter and CCDC-Code.

Sample	Machine	Source	Temp.	Detector Distance	Time/ Frame	#Frames	Frame width	CCDC
	Bruker		[K]	[mm]	[s]		[°]	
H2*	D8	Mo	100	30	20	2537	0.500	2018340
N1	D8	Mo	100	30	3	1357	0.500	2018344
N2	D8	Mo	100	30	2	1005	0.500	2018351
N3	D8	Mo	300	30	10	3018	0.500	2018342
N4	D8	Mo	200	30	5	670	1.000	2018343
N5	D8	Mo	100	30	5	1584	0.500	2018345
N6	D8	Mo	150	30	20	1070	1.000	2018341
P1	D8	Cu	100	30	10	8978	0.500	2018356
P2	D8	Mo	100	30	10	618	1.000	2018353
P3	D8	Mo	120	30	10	1439	0.500	2018355
P4	D8	Mo	120	30	30	1559	0.500	2018352
S2	D8	Mo	100	30	10	2272	0.500	2018354

Bis[((1-benzyl-2-methyl-3-(oxo-κO)-pyridine-4(1H)-thionato-κS)(η6-p-cymene) ruthenium(II)) iodide] (H3*)

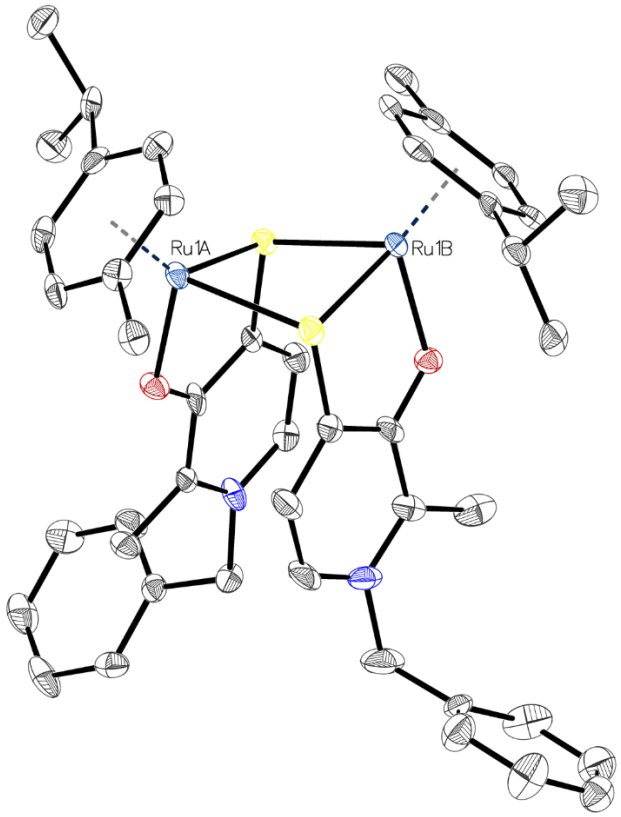

Fig. S37 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.0105Å. Hydrogen atoms, solvent and counter ion omitted for clarity.

Table S2 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	4	Measurement method	\f and \w scans
Crystal habit	clear red block	a [Å]	19.6766(16)		
Crystal size [mm^3]	0.06 × 0.04 × 0.01	b [Å]	10.0026(10)	Abs. correction type	multiscan
Empirical formula	C47H56I2N2O3Ru2S2	c [Å]	24.018(2)	Abs. correction Tmin	0.6503
Formula weight [g/mol]	1216.99	α [°]	90	Abs. correction Tmax	0.7460
Temperature [K]	100.0	β [°]	92.308(4)	Density (calculated) [g/cm^3]	1.711
Crystal system	monoclinic	γ [°]	90	Absorption coefficient [mm^{-1}]	2.076
Space group	P21/c	Volume [Å^3]	4723.2(8)	F (000) [e$^-$]	2408.0

Table S3 Data collection and structure refinement.

2Θ range for data collection [°]	4.412 to 50.7	Index ranges		Goodness-of-fit on F^2	0.993
Reflections collected	20806	h	$-23 \le h \le 22$	Diff. peak and hole [$e^{-}Å^{-3}$]	1.20/-0.72
Data / restraints / parameters	8473/0/533	k	$-11 \le k \le 12$		
Refinement method	Intrinsic Phasing	l	$-28 \le l \le 28$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0815, wR2 = 0.0808	Weighting scheme	where
		I>2σ(I)	R1 = 0.0462, wR2 = 0.0965	$w=1/[\sigma^2(Fo^2) + (0.0056P)^2]$	$P=(F_o^2+2F_c^2)/3$

[(1-Methyl-1H-imidazole-κN3)(1,2-dimethyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)(η6-p-cymene)ruthenium(II)] hexafluorophosphate (N1)

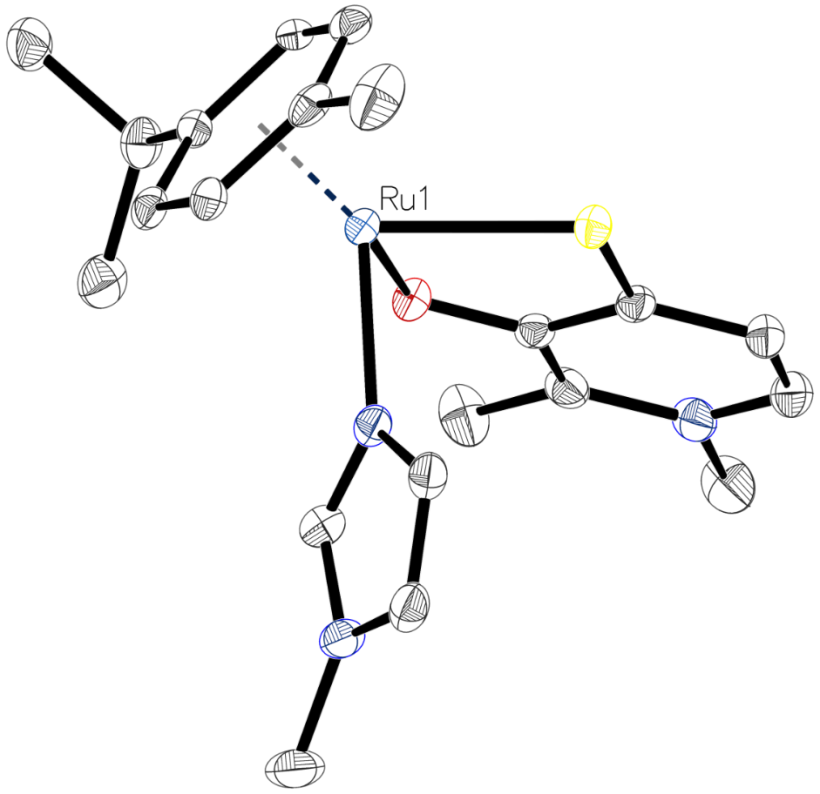

Fig. S38 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.0060Å. Hydrogen atoms and counter ion omitted for clarity. Because of disorder, part B omitted, main disorder residue 37%.

Table S4 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	2	Measurement method	\f and \w scans
Crystal habit	clear orange block	a [Å]	9.5074(2)		
Crystal size [mm³]	0.16 × 0.16 × 0.12	b [Å]	10.0971(3)	Abs. correction type	multiscan
Empirical formula	C21H28F6N3OPRuS	c [Å]	13.5952(4)	Abs. correction Tmin	0.4548
Formula weight [g/mol]	616.56	α [°]	74.3060(9)	Abs. correction Tmax	0.4932
Temperature [K]	100.0	β [°]	77.5332(9)	Density (calculated) [g/cm³]	1.669
Crystal system	triclinic	γ [°]	87.8246(11)	Absorption coefficient [mm⁻¹]	0.855
Space group	P-1	Volume [Å³]	1226.53(6)	F (000) [e⁻]	624.0

Table S5 Data collection and structure refinement.

2Θ range for data collection [°]	4.532 to 50.698	Index ranges		Goodness-of-fit on F^2	1.029
Reflections collected	28348	h	$-11 \le h \le 11$	Diff. peak and hole [$e^{-}Å^{-3}$]	1.64/-1.92
Data / restraints / parameters	4483/138/396	k	$-12 \le k \le 12$		
Refinement method	Patterson Method	l	$-16 \le l \le 16$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0455, wR2 = 0.1089	Weighting scheme	where
		I>2σ(I)	R1 = 0.0442, wR2 = 0.1079	$w=1/[\sigma^2(Fo^2) + (0.0505P)^2 + 6.4440P]$	$P=(F_o^2+2F_c^2)/3$

[(1-Methyl-1H-imidazole-κN3)(1,2-dimethyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)(η5-1,2,3,4,5-pentamethylcyclopentadienyl)rhodium(III)] hexafluorophosphate (N2)

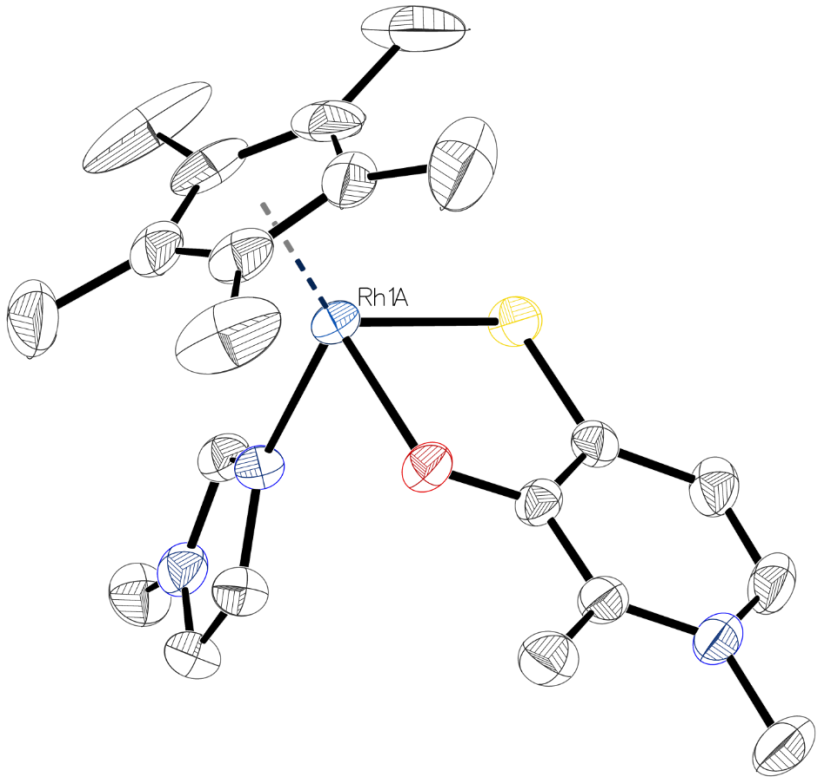

Fig. S39 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.0062Å. Hydrogen atoms, counter ion and second independent molecule omitted for clarity.

Table S6 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	4	Measurement method	\f and \w scans
Crystal habit	clear red block	a [Å]	8.7282(5)		
Crystal size [mm³]	0.22 × 0.22 × 0.18	b [Å]	16.3364(10)	Abs. correction type	multiscan
Empirical formula	C21H29F6N3OPRhS	c [Å]	17.8947(11)	Abs. correction Tmin	0.5061
Formula weight [g/mol]	619.41	α [°]	93.913(2)	Abs. correction Tmax	0.6026
Temperature [K]	100.0	β [°]	97.756(3)	Density (calculated) [g/cm³]	1.632
Crystal system	triclinic	γ [°]	90.927(3)	Absorption coefficient [mm^{-1}]	0.887
Space group	P-1	Volume [Å³]	2521.5(3)	F (000) [e$^-$]	1256.0

Table S7 Data collection and structure refinement.

2Θ range for data collection [°]	4.606 to 52.108	Index ranges		Goodness-of-fit on F^2	1.036
Reflections collected	43998	h	$-9 \le h \le 10$	Diff. peak and hole [$e^{-}Å^{-3}$]	0.49/-1.12
Data / restraints / parameters	9914/0/629	k	$-20 \le k \le 20$		
Refinement method	Patterson Method	l	$-22 \le l \le 22$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0511, wR2 = 0.1097	Weighting scheme	where
		I>2σ(I)	R1 = 0.0429, wR2 = 0.1029	$w=1/[\sigma^2(Fo^2) + (0.0379P)^2 + 4.2723P]$	$P=(F_o^2+2F_c^2)/3$

[(1-Methyl-1H-imidazole-κN3)(1,2-dimethyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)(η5-1,2,3,4,5-pentamethylcyclopentadienyl)iridium(III)] hexafluorophosphate (N3)

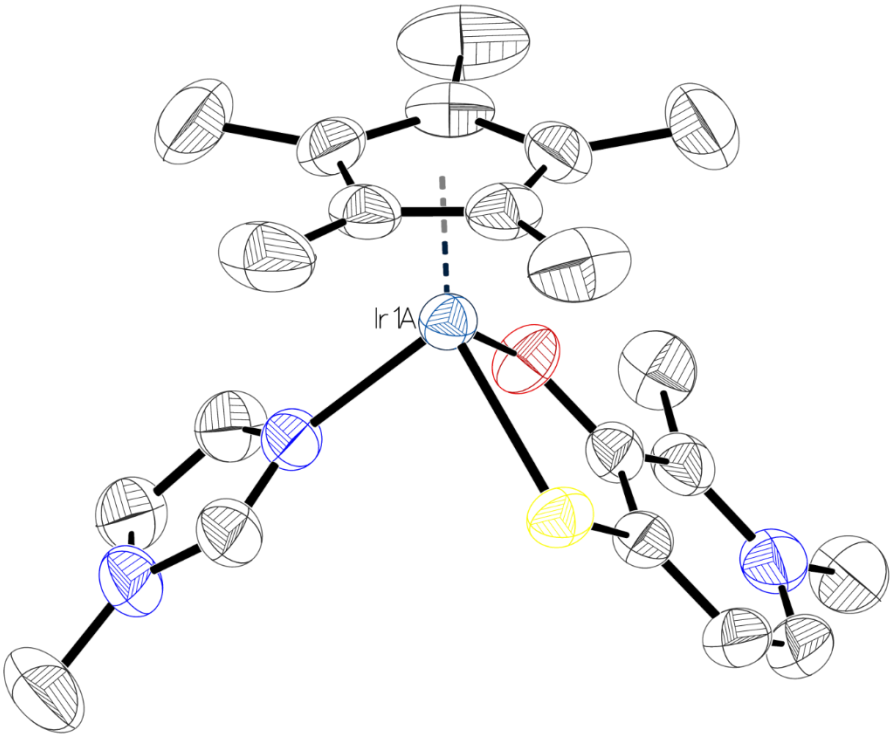

Fig. S40 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.0046Å. Hydrogen atoms, counter ion and second independent molecule omitted for clarity.

Table S8 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	4	Measurement method	\f and \w scans
Crystal habit	clear orange block	a [Å]	8.77040(10)		
Crystal size [mm^3]	0.12 × 0.1 × 0.07	b [Å]	16.4092(2)	Abs. correction type	multiscan
Empirical formula	C21H29F6IrN3OPS	c [Å]	18.0771(3)	Abs. correction Tmin	0.6252
Formula weight [g/mol]	708.70	α [°]	93.7892(5)	Abs. correction Tmax	0.7457
Temperature [K]	300.0	β [°]	97.5756(5)	Density (calculated) [g/cm^3]	1.830
Crystal system	triclinic	γ [°]	90.7492(5)	Absorption coefficient [mm^{-1}]	5.396
Space group	P-1	Volume [Å^3]	2572.60(6)	F (000) [e$^-$]	1384.0

Table S9 Data collection and structure refinement.

2Θ range for data collection [°]	4.932 to 50.7	Index ranges		Goodness-of-fit on F^2	1.053
Reflections collected	137892	h	$-10 \le h \le 10$	Diff. peak and hole [$e^{-}Å^{-3}$]	0.51/-0.45
Data / restraints / parameters	9400/140/724	k	$-19 \le k \le 19$		
Refinement method	Direct Methods	l	$-21 \le l \le 21$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0181, wR2 = 0.0404	Weighting scheme	where
		I>2σ(I)	R1 = 0.0166, wR2 = 0.0396	$w=1/[\sigma^2(Fo^2) + (0.0172P)^2 + 2.3922P]$	$P=(F_o^2+2F_c^2)/3$

[(1-Methyl-1H-imidazole-κN3)(1-benzyl-2-methyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)(η6-p-cymene)ruhtenium(II)] hexafluorophosphate (N4)

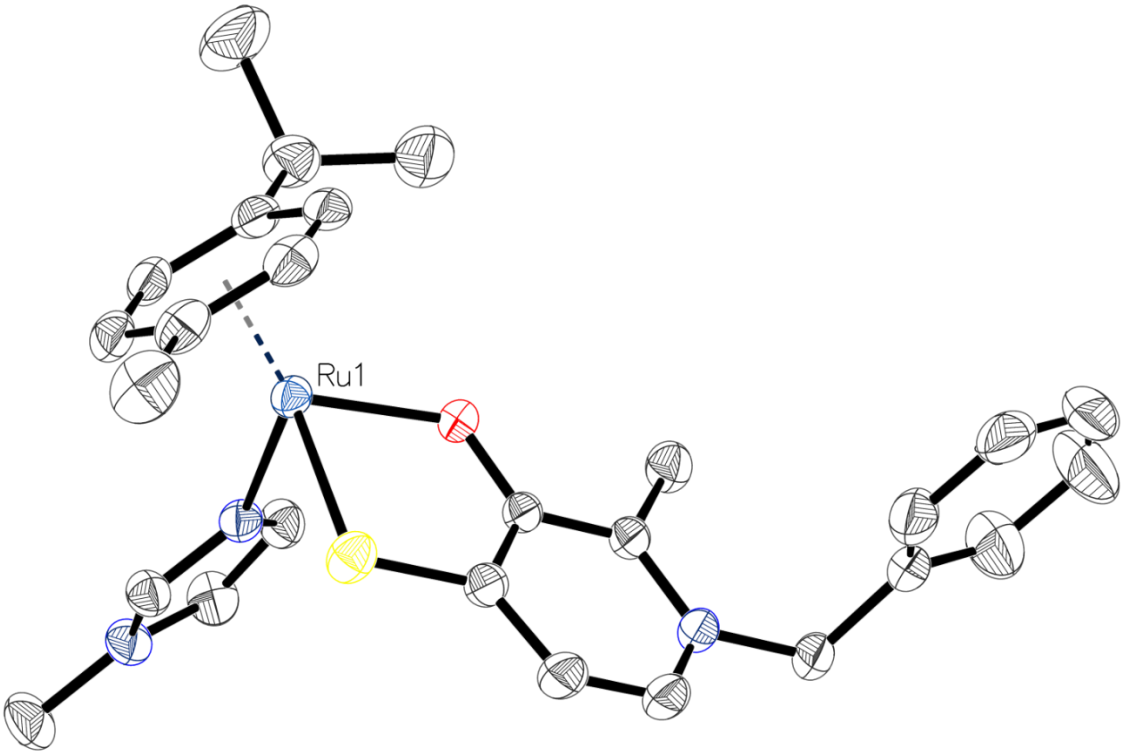

Fig. S41 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.00 Å. Hydrogen atoms and counter ion omitted for clarity.

Table S10 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	2	Measurement method	\f and \w scans
Crystal habit	clear orange block	a [Å]	10.3415(3)		
Crystal size [mm^3]	0.2 × 0.06 × 0.06	b [Å]	11.8930(3)	Abs. correction type	multiscan
Empirical formula	C27H32F6N3OPRuS	c [Å]	13.3257(4)	Abs. correction Tmin	0.5351
Formula weight [g/mol]	692.65	α [°]	67.1050(10)	Abs. correction Tmax	0.5642
Temperature [K]	200.0	β [°]	88.0280(10)	Density (calculated) [g/cm^3]	1.569
Crystal system	triclinic	γ [°]	76.6230(10)	Absorption coefficient [mm^{-1}]	0.725
Space group	P-1	Volume [Å^3]	1466.04(7)	F (000) [e$^-$]	704.0

Table S11 Data collection and structure refinement.

2Θ range for data collection [°]	5.148 to 60.092	Index ranges		Goodness-of-fit on F^2	1.099
Reflections collected	48628	h	$-14 \le h \le 14$	Diff. peak and hole [$e^{-}Å^{-3}$]	1.59/-0.75
Data / restraints / parameters	8564/0/366	k	$-16 \le k \le 15$		
Refinement method	Intrinsic Phasing	l	$-18 \le l \le 18$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0439, wR2 = 0.0974	Weighting scheme	where
		I>2σ(I)	R1 = 0.0374, wR2 = 0.0927	$w=1/[\sigma^2(Fo^2) + (0.0372P)^2 +1.9551P]$	$P=(F_o^2+2F_c^2)/3$

[(1-Methyl-1H-imidazole-κN3)(1-benzyl-2-methyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)(η5-1,2,3,4,5-pentamethylcyclopentadienyl)rhodium(III)] hexafluorophosphate (N5)

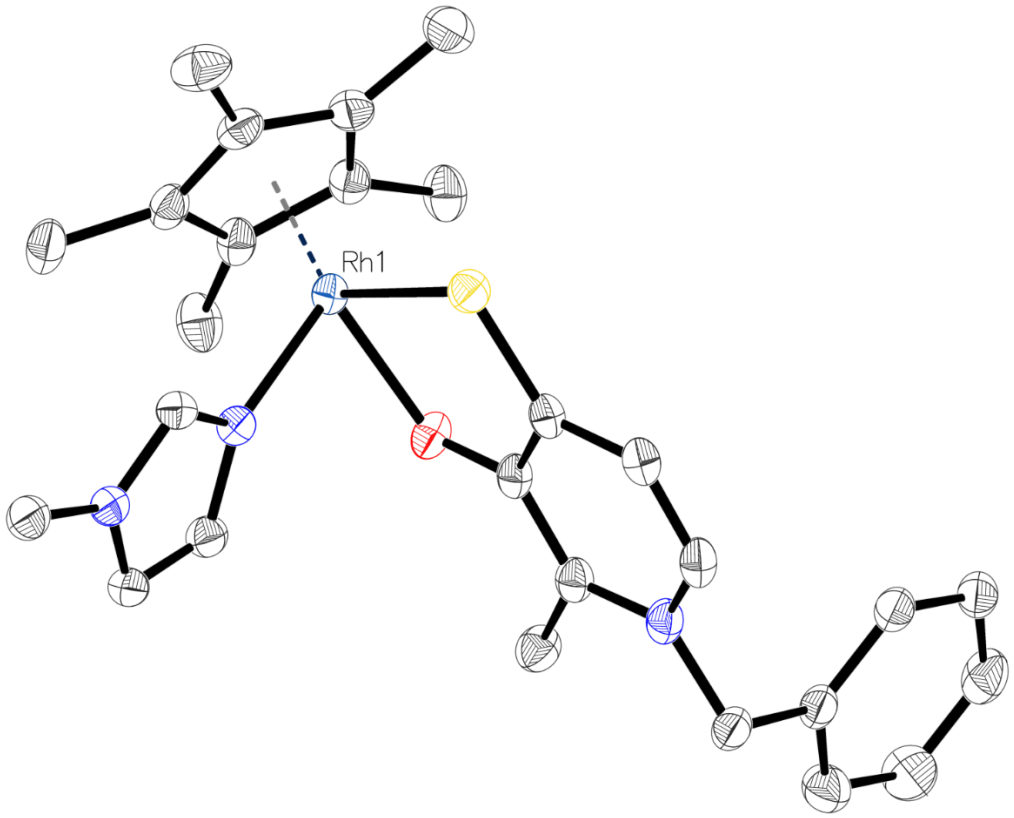

Fig. S42 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.0029 Å. Hydrogen atoms and counter ion omitted for clarity.

Table S12 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	2	Measurement method	\f and \w scans
Crystal habit	clear red block	a [Å]	9.8382(3)		
Crystal size [mm³]	0.2 × 0.1 × 0.06	b [Å]	12.2093(4)	Abs. correction type	multiscan
Empirical formula	C27H33F6N3OPRhS	c [Å]	14.1367(5)	Abs. correction Tmin	0.0684
Formula weight [g/mol]	695.50	α [°]	67.1738(11)	Abs. correction Tmax	0.0990
Temperature [K]	100.0	β [°]	80.8485(12)	Density (calculated) [g/cm³]	1.589
Crystal system	triclinic	γ [°]	68.3017(11)	Absorption coefficient [mm⁻¹]	0.779
Space group	P-1	Volume [Å³]	1453.95(8)	F (000) [e⁻]	708.0

Table S13 Data collection and structure refinement.

2Θ range for data collection [°]	4.802 to 56.558	Index ranges		Goodness-of-fit on F^2	1.038
Reflections collected	50283	h	$-13 \le h \le 13$	Diff. peak and hole [$e^{-}Å^{-3}$]	1.50/-1.46
Data / restraints / parameters	7183/0/368	k	$-16 \le k \le 16$		
Refinement method	Direct Methods	l	$-18 \le l \le 18$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0354, wR2 = 0.0565	Weighting scheme	where
		I>2σ(I)	R1 = 0.0278, wR2 = 0.0517	$w=1/[\sigma^2(Fo^2) + (0.0165P)^2 + 1.3956P]$	$P=(F_o^2+2F_c^2)/3$

[(1-Methyl-1H-imidazole-κN3)(1-benzyl-2-methyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)(η5-1,2,3,4,5-pentamethylcyclopentadienyl)iridium(III)] hexafluorophosphate (N6)

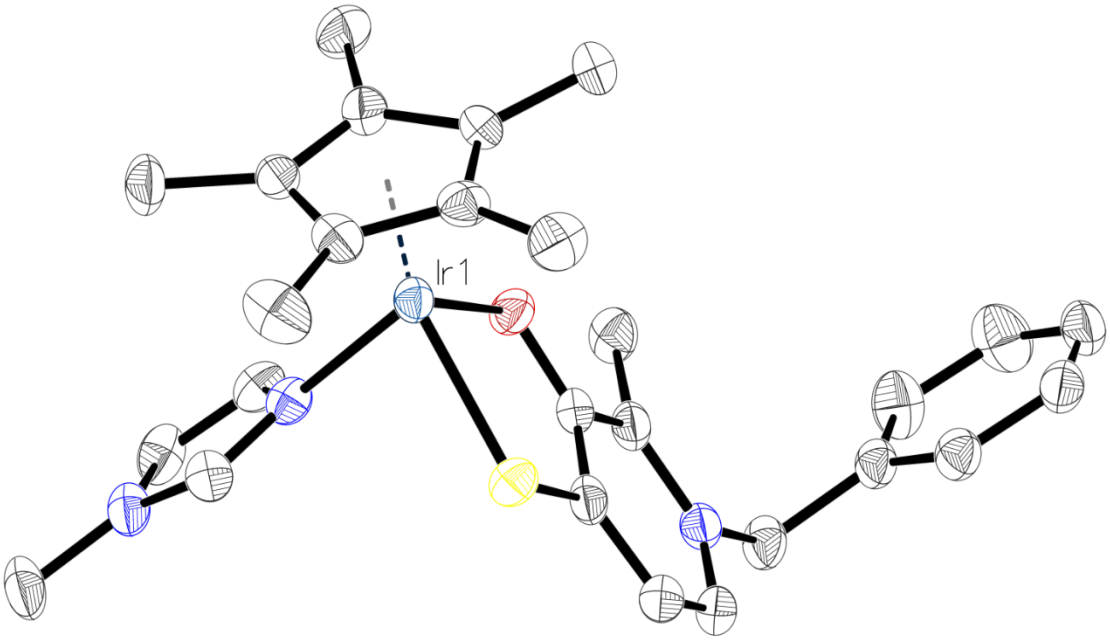

Fig. S43 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.0085 Å. Hydrogen atoms and counter ion omitted for clarity.

Table S14 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	2	Measurement method	\f and \w scans
Crystal habit	clear red block	a [Å]	9.8020(5)		
Crystal size [mm^3]	0.117 × 0.113 × 0.019	b [Å]	12.3228(6)	Abs. correction type	multiscan
Empirical formula	C27H33F6IrN3OPS	c [Å]	13.9774(7)	Abs. correction Tmin	0.4642
Formula weight [g/mol]	784.79	α [°]	68.0585(16)	Abs. correction Tmax	0.5642
Temperature [K]	150.0	β [°]	81.3239(17)	Density (calculated) [g/cm^3]	1.778
Crystal system	triclinic	γ [°]	69.4402(17)	Absorption coefficient [mm^{-1}]	4.744
Space group	P-1	Volume [Å^3]	1465.89(13)	F (000) [e$^-$]	772.0

Table S15 Data collection and structure refinement.

2Θ range for data collection [°]	4.44 to 50.7	Index ranges		Goodness-of-fit on F^2	1.085
Reflections collected	51281	h	$-11 \leq h \leq 11$	Diff. peak and hole [$e^{-}Å^{-3}$]	1.04/-1.51
Data / restraints / parameters	5360/0/368	k	$-14 \leq k \leq 14$		
Refinement method	Patterson Method	l	$-16 \leq l \leq 16$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0395, wR2 = 0.0630	Weighting scheme	where
		I>2σ(I)	R1 = 0.0306, wR2 = 0.0591	$w=1/[\sigma^2(Fo^2) + 7.5117P]$	$P=(F_o^2+2F_c^2)/3$

[(1,3,5-Triaza-7-phosphaadamantane-κP)(1,2-Dimethyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)(η6-p-cymene)ruhtenium(II)] hexafluorophosphate (P1)

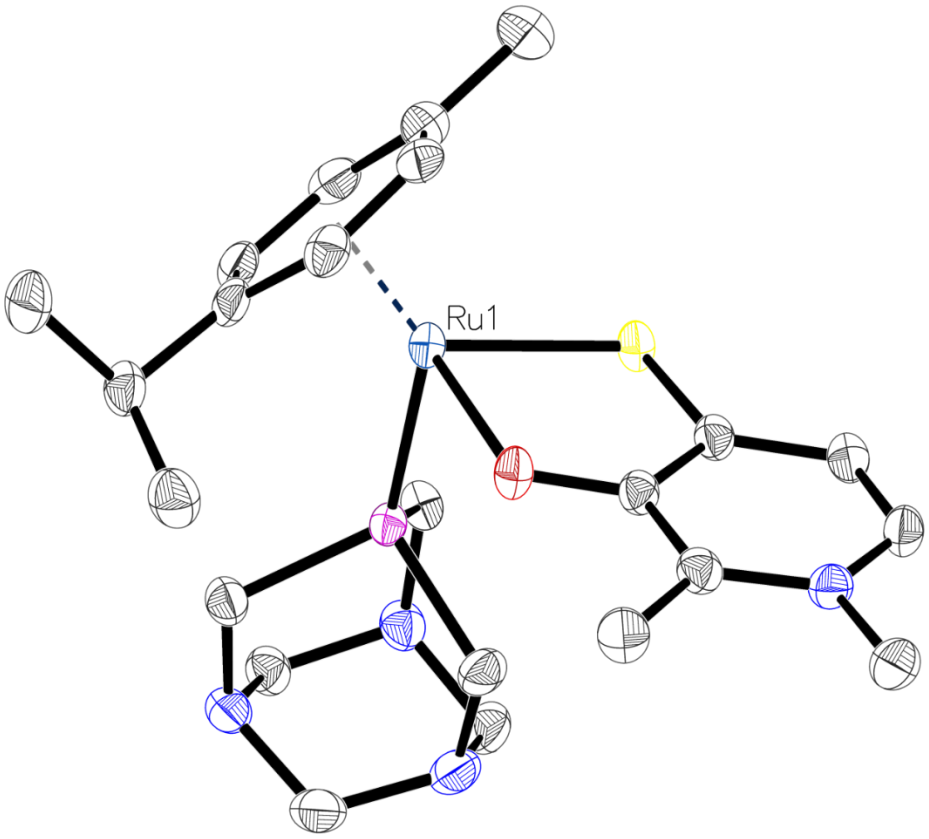

Fig. S44 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.00 Å. Hydrogen atoms and counter ion omitted for clarity.

Table S16 Sample and crystal data.

Radiation [Å]	CuKα (λ = 1.54178)	Z	2	Measurement method	\f and \w scans
Crystal habit	clear red block	a [Å]	8.8476(5)		
Crystal size [mm^3]	0.03 × 0.02 × 0.02	b [Å]	11.4425(6)	Abs. correction type	multiscan
Empirical formula	C23H34F6N4OP2RuS	c [Å]	13.8462(7)	Abs. correction Tmin	0.6929
Formula weight [g/mol]	691.61	α [°]	82.475(2)	Abs. correction Tmax	0.7536
Temperature [K]	100.0	β [°]	79.907(2)	Density (calculated) [g/cm^3]	1.679
Crystal system	triclinic	γ [°]	88.353(3)	Absorption coefficient [mm^{-1}]	7.061
Space group	P-1	Volume [Å^3]	1368.17(13)	F (000) [e$^-$]	704.0

Table S17 Data collection and structure refinement.

2Θ range for data collection [°]	6.538 to 145.224	Index ranges		Goodness-of-fit on F^2	1.058
Reflections collected	33825	h	$-10 \le h \le 10$	Diff. peak and hole [$e^{-}Å^{-3}$]	1.21/-0.61
Data / restraints / parameters	5339/72/388	k	$-14 \le k \le 14$		
Refinement method	Direct Methods	l	$-17 \le l \le 17$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0283, wR2 = 0.0684	Weighting scheme	where
		I>2σ(I)	R1 = 0.0259, wR2 = 0.0655	$w=1/[\sigma^2(Fo^2) + (0.0310P)^2 + 1.2560P]$	$P=(F_o^2+2F_c^2)/3$

[(1,3,5-Triaza-7-phosphaadamantane-κP)(1,2-Dimethyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)(η5-1,2,3,4,5-pentamethylcyclopentadienyl)rhodium(III)] hexafluorophosphate (P2)

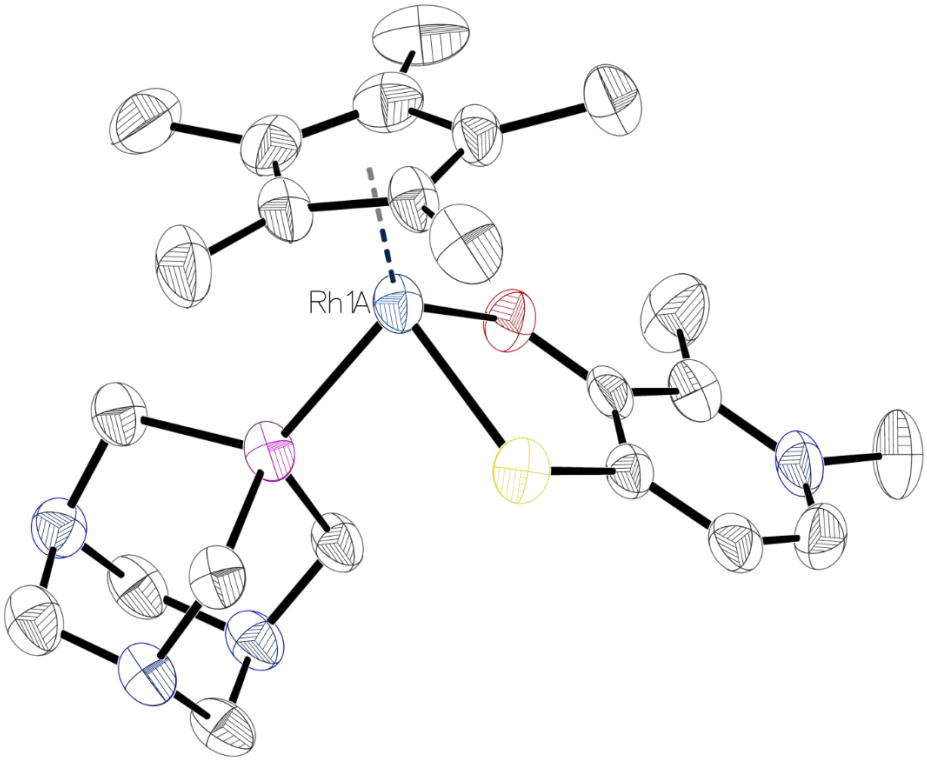

Fig. S45 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.0140 Å. Hydrogen atoms, counter ion and second independent molecule omitted for clarity. Squeeze was used because high degree of disorder. According voids contain 589.8 $Å^3$ with 173.2 e^-. Anion residue disorder 86%.

Table S18 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	8	Measurement method	\f and \w scans
Crystal habit	clear orange plate	a [Å]	21.070(3)		
Crystal size [mm^3]	0.2 × 0.18 × 0.01	b [Å]	9.9943(14)	Abs. correction type	multiscan
Empirical formula	C23H34.5F6N4OP2RhS	c [Å]	31.846(4)	Abs. correction Tmin	0.3790
Formula weight [g/mol]	693.95	α [°]	90	Abs. correction Tmax	0.4901
Temperature [K]	100.0	β [°]	99.318(5)	Density (calculated) [g/cm^3]	1.393
Crystal system	monoclinic	γ [°]	90	Absorption coefficient [mm^{-1}]	0.731
Space group	P21/c	Volume [$Å^3$]	6617.8(17)	F (000) [e^-]	2828.0

Table S19 Data collection and structure refinement.

2Θ range for data collection [°]	4.334 to 0.88	Index ranges		Goodness-of-fit on F^2	0.999
Reflections collected	40832	h	$-25 \leq h \leq 25$	Diff. peak and hole [$e^{-}Å^{-3}$]	0.97/-1.06
Data / restraints / parameters	12176/55/687	k	$-12 \leq k \leq 12$		
Refinement method	Direct Methods	l	$-38 \leq l \leq 38$	Function minimized	$\Sigma w (F_o^2 - F_c^2)^2$
		all data	R1 = 0.1402, wR2 = 0.2061	Weighting scheme	where
		I>2σ(I)	R1 = 0.0732, wR2 = 0.1667	$w=1/[\sigma^2(Fo^2) + (0.0891P)^2]$	$P=(F_o^2+2F_c^2)/3$

[(1,3,5-Triaza-7-phosphaadamantane-κP)(1-benzyl-2-methyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)(η6-p-cymene)ruthenium(II)] hexafluorophosphate (P3)

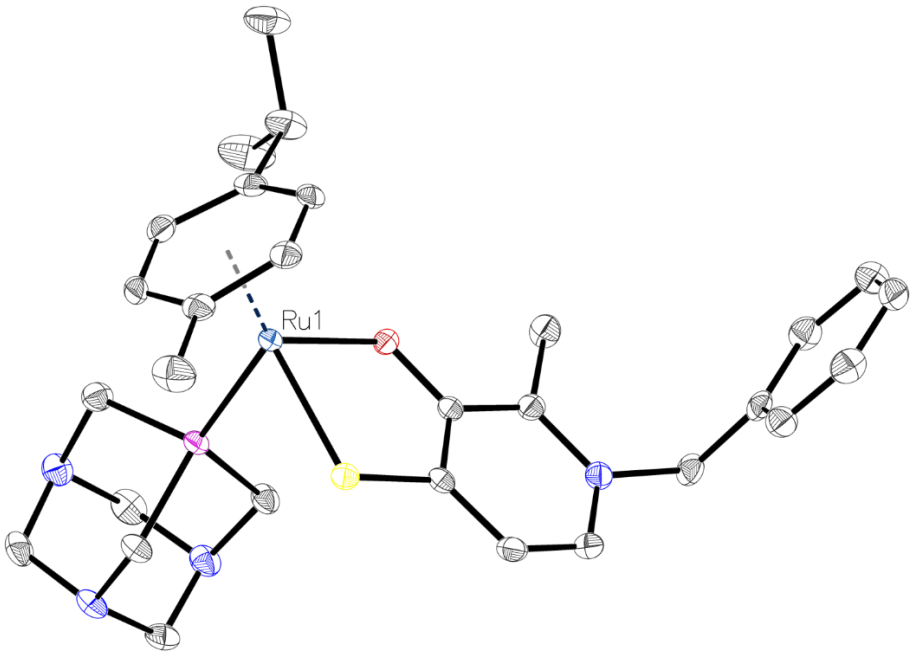

Fig. S46 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.0040 Å. Hydrogen atoms, solvent and counter ion omitted for clarity.

Table S20 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	2	Measurement method	\f and \w scans
Crystal habit	clear orange block	a [Å]	12.3099(3)		
Crystal size [mm^3]	0.06 × 0.04 × 0.01	b [Å]	12.4123(4)	Abs. correction type	multiscan
Empirical formula	C31H42Cl4F6N4OP2RuS	c [Å]	14.4636(4)	Abs. correction Tmin	0.5221
Formula weight [g/mol]	940.58	α [°]	65.2024(11)	Abs. correction Tmax	0.5642
Temperature [K]	120.0	β [°]	70.4638(11)	Density (calculated) [g/cm^3]	1.660
Crystal system	triclinic	γ [°]	77.0040(11)	Absorption coefficient [mm^{-1}]	0.904
Space group	P-1	Volume [Å^3]	1881.42(9)	F (000) [e$^-$]	958.0

Table S21 Data collection and structure refinement.

2Θ range for data collection [°]	4.306 to 50.696	Index ranges		Goodness-of-fit on F^2	0.997
Reflections collected	43194	h	$-14 \le h \le 14$	Diff. peak and hole [$e^{-}Å^{-3}$]	1.73/-0.81
Data / restraints / parameters	6887/2/483	k	$-14 \le k \le 14$		
Refinement method	Direct Methods	l	$-17 \le l \le 17$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0335, wR2 = 0.0757	Weighting scheme	where
		I>2σ(I)	R1 = 0.0303, wR2 = 0.0732	$w=1/[\sigma^2(Fo^2) + (0.338P)^2 +3.7448P]$	$P=(F_o^2+2F_c^2)/3$

[(1,3,5-Triaza-7-phosphaadamantane-κP)(1-benzyl-2-methyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)(η5-1,2,3,4,5-pentamethylcyclopentadienyl)rhodium(III)] hexafluorophosphate (P4)

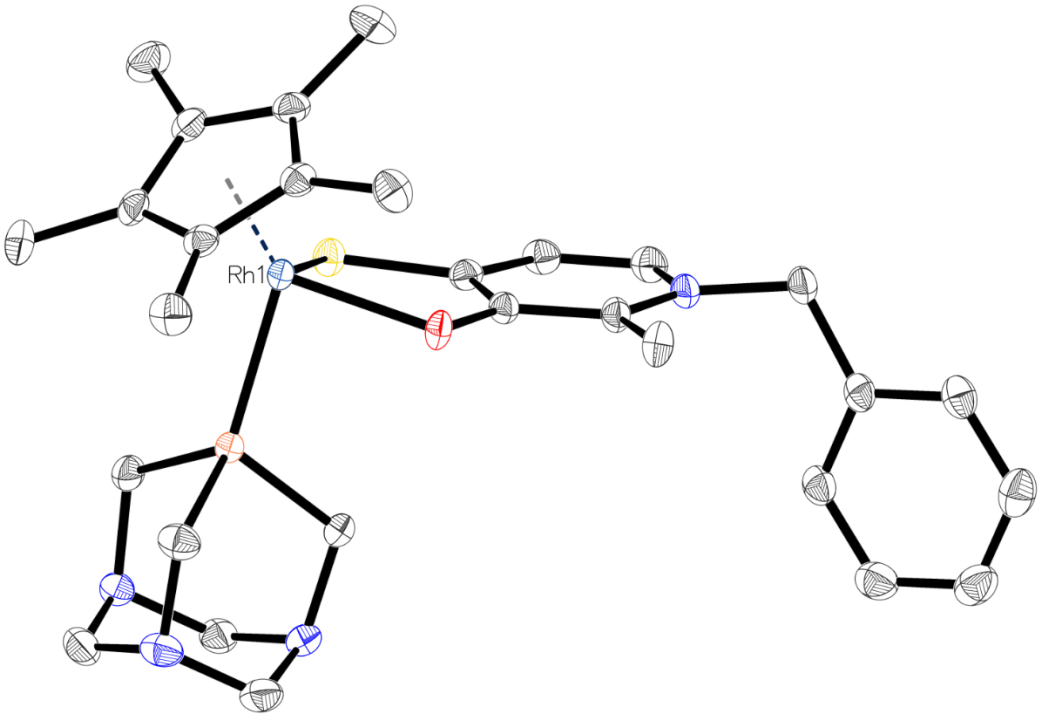

Fig. S47 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.0039 Å. Hydrogen atoms and counter ion omitted for clarity.

Table S22 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	2	Measurement method	\f and \w scans
Crystal habit	clear orange block	a [Å]	9.4865(4)		
Crystal size [mm³]	0.108 × 0.085 × 0.046	b [Å]	13.5259(8)	Abs. correction type	multiscan
Empirical formula	C29H39F6N4OP2RhS	c [Å]	13.5730(8)	Abs. correction Tmin	0.7142
Formula weight [g/mol]	770.55	α [°]	68.784(2)	Abs. correction Tmax	0.7460
Temperature [K]	120.0	β [°]	84.539(3)	Density (calculated) [g/cm³]	4.611
Crystal system	triclinic	γ [°]	78.200(3)	Absorption coefficient [mm⁻¹]	0.770
Space group	P-1	Volume [Å³]	1588.82(15)	F (000) [e⁻]	788.0

Table S23 Data collection and structure refinement.

2Θ range for data collection [°]	4.388 to 60.068	Index ranges		Goodness-of-fit on F^2	1.053
Reflections collected	52261	h	$-13 \le h \le 13$	Diff. peak and hole [$e^{-}Å^{-3}$]	0.96/-0.99
Data / restraints / parameters	9290/0/403	k	$-19 \le k \le 19$		
Refinement method	Direct Methods	l	$-19 \le l \le 19$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0495, wR2 = 0.0866	Weighting scheme	where
		I>2σ(I)	R1 = 0.0373, wR2 = 0.0793	$w=1/[\sigma^2(Fo^2) + (0.0308P)^2 + 2.3738P]$	$P=(F_o^2+2F_c^2)/3$

[(Thioatocarbonyldiamine-κS)(1-benzyl-2-methyl-3-oxo-κO-pyridine-4(1H)-thionato-κS)](η6-p-cymene)ruthenium(II)] chloride (S2)

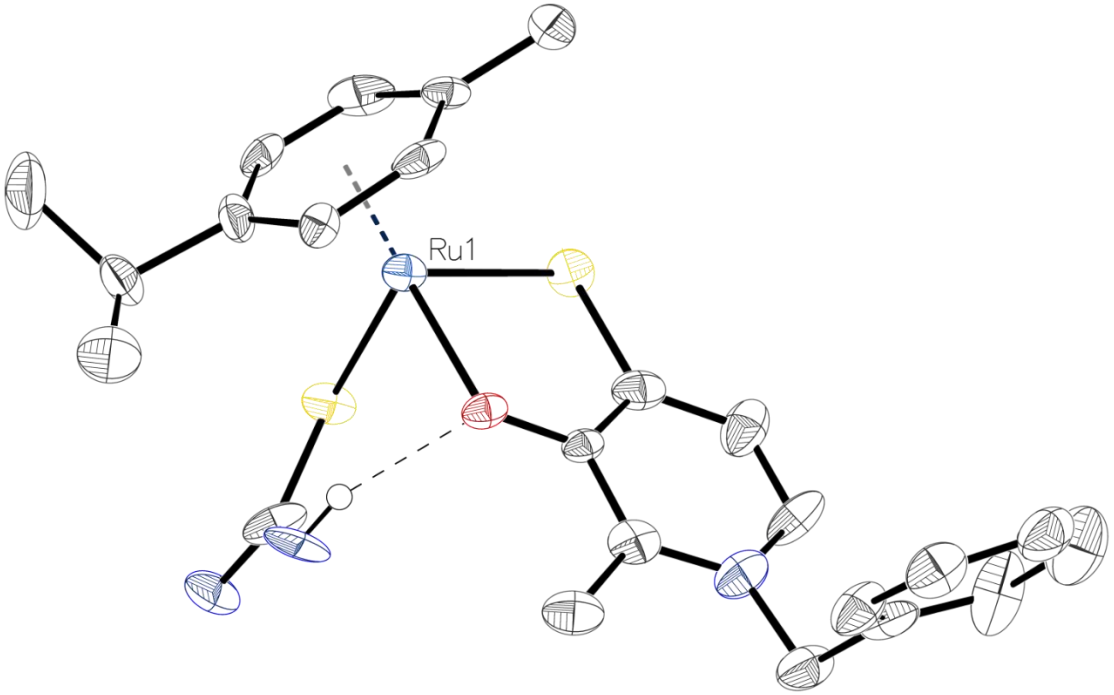

Fig. S48 Crystal structure, drawn with 50% displacement ellipsoid. The bond precision for C-C single bonds is 0.0286 Å. Hydrogen atoms and counter ion omitted for clarity.

Table S24 Sample and crystal data.

Radiation [Å]	MoKα (λ = 0.71073)	Z	2	Measurement method	\f and \w scans
Crystal habit	clear orange plate	a [Å]	10.107(2)		
Crystal size [mm³]	0.2 × 0.14 × 0.03	b [Å]	11.107(2)	Abs. correction type	multiscan
Empirical formula	C24H30ClN3ORuS2	c [Å]	12.096(2)	Abs. correction Tmin	0.841
Formula weight [g/mol]	577.15	α [°]	90	Abs. correction Tmax	0.974
Temperature [K]	100.0	β [°]	108.775(8)	Density (calculated) [g/cm³]	1.491
Crystal system	monoclinic	γ [°]	90	Absorption coefficient [mm^{-1}]	0.897
Space group	P21	Volume [Å³]	1285.7(4)	F (000) [e$^-$]	592.0

Table S25 Data collection and structure refinement.

2Θ range for data collection [°]	4.586 to 51.362	Index ranges		Goodness-of-fit on F^2	1.171
Reflections collected	4869	h	$-12 \le h \le 11$	Diff. peak and hole [$e^{-}Å^{-3}$]	1.62/-1.33
Data / restraints / parameters	4758/7/293	k	$-13 \le k \le 13$		
Refinement method	Direct Methods	l	$0 \le l \le 14$	Function minimized	$\Sigma\, w\,(F_o^2 - F_c^2)^2$
		all data	R1 = 0.0671, wR2 = 0.1833	Weighting scheme	where
		I>2σ(I)	R1 = 0.0649, wR2 = 0.1821	$w=1/[\sigma^2(Fo^2) + (0.0144P)^2 + 21.4891P]$	$P=(F_o^2+2F_c^2)/3$

UV Vis

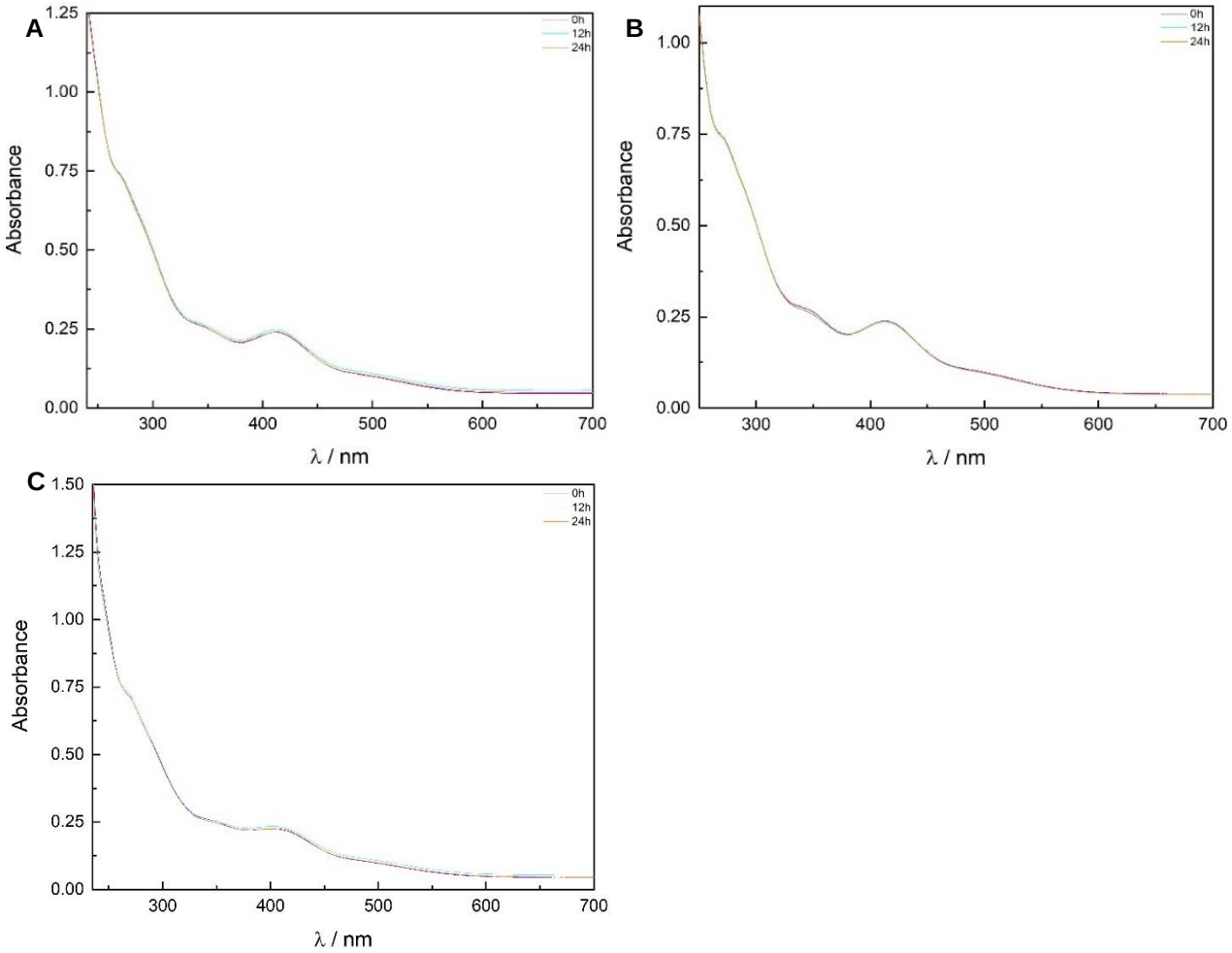

Fig. S49 UV-Vis spectra of complexes **H1** (**A**), **H2** (**B**) and **H3** (**C**) recorded over 24 h in PBS at 25 °C.

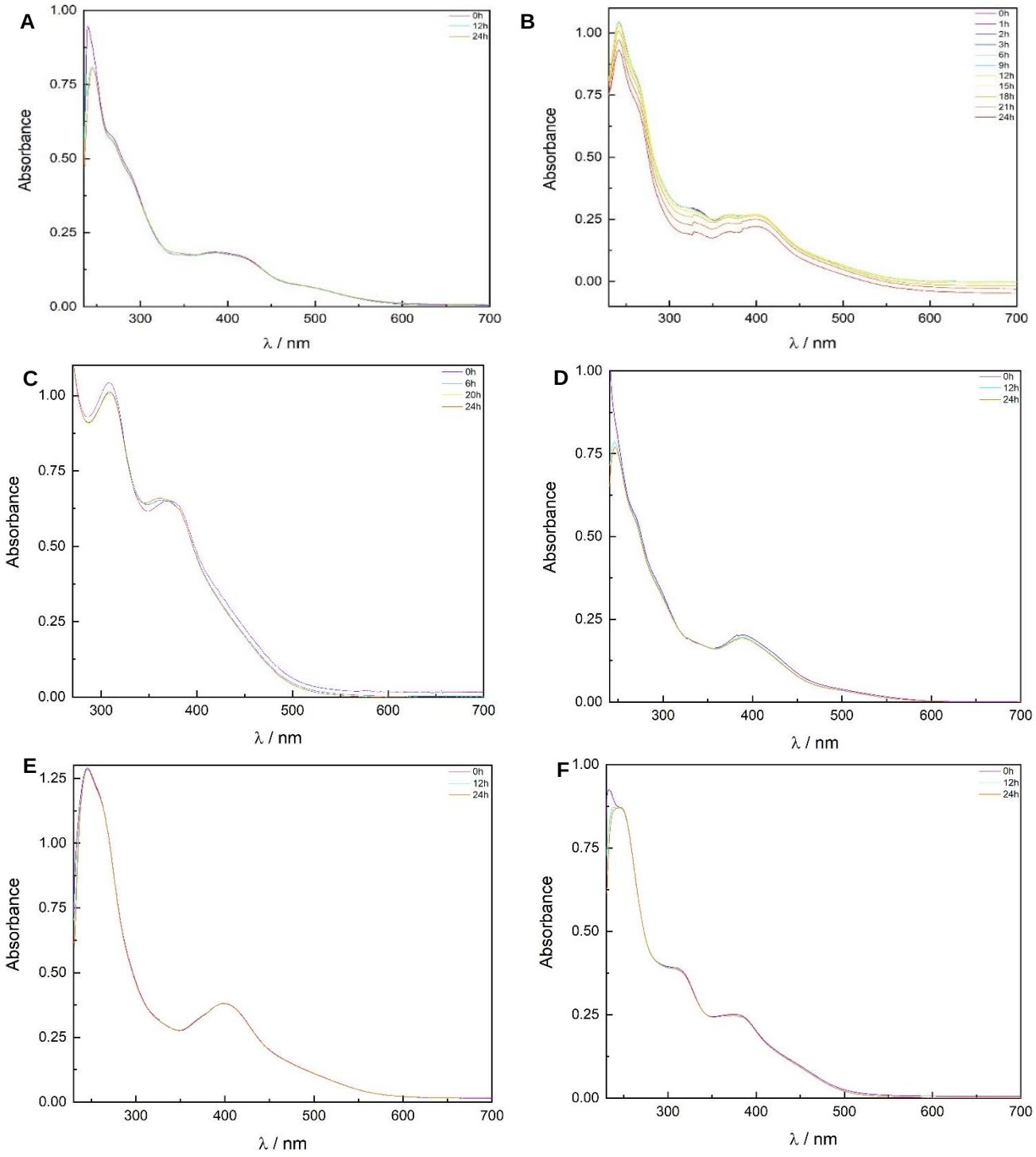

Fig. S50 UV Vis spectra of complexes **N1** (**A**), **N2** (**B**), **N3** (**C**), **N4** (**D**), **N5** (**E**) and **N6** (**F**) recorded over 24 h in PBS at 25 °C.

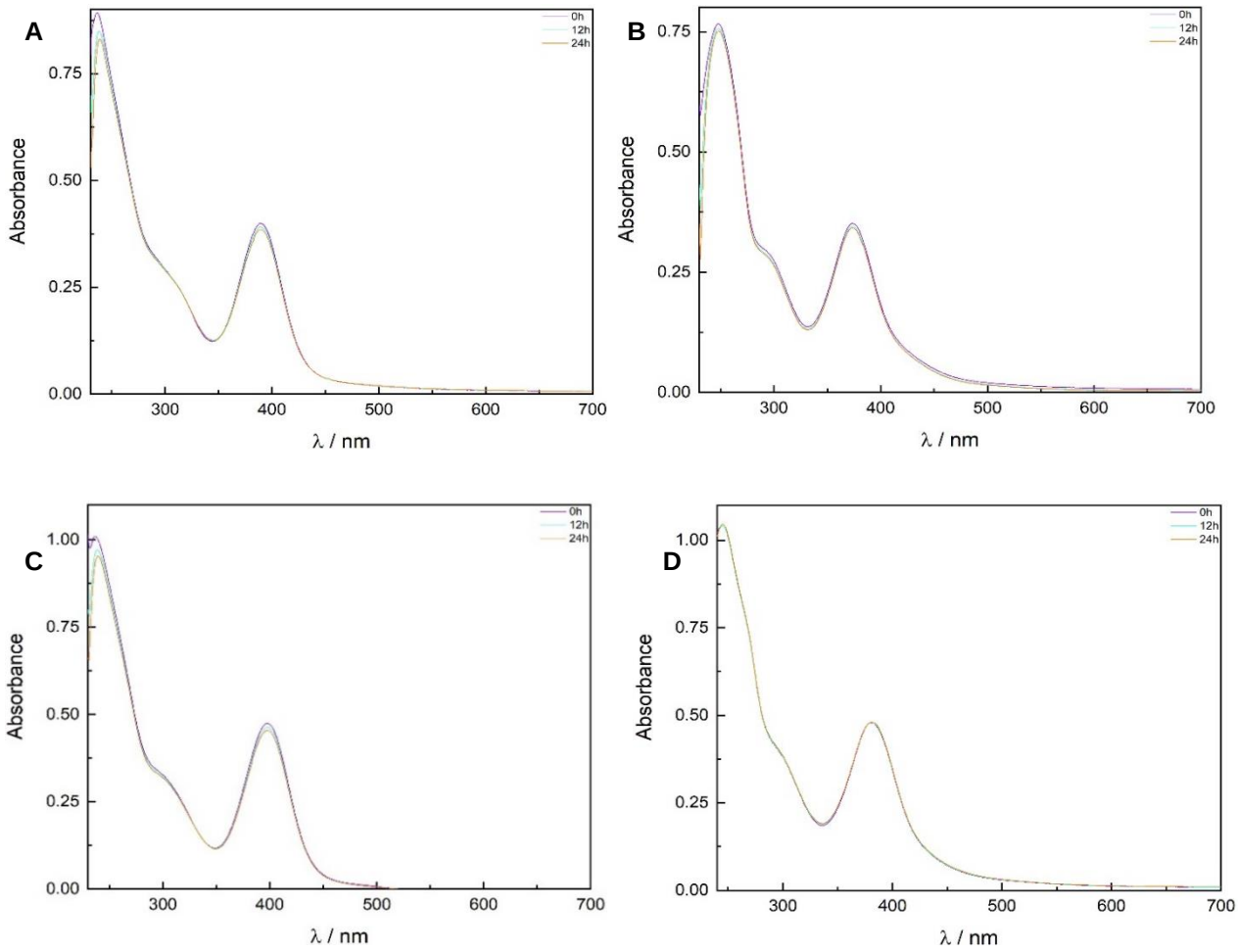

Fig. S51 UV Vis spectra of complexes **P1** (**A**), **P2** (**B**), **P3** (**C**), and **P4** (**D**) recorded over 24 h in PBS at 25 °C.

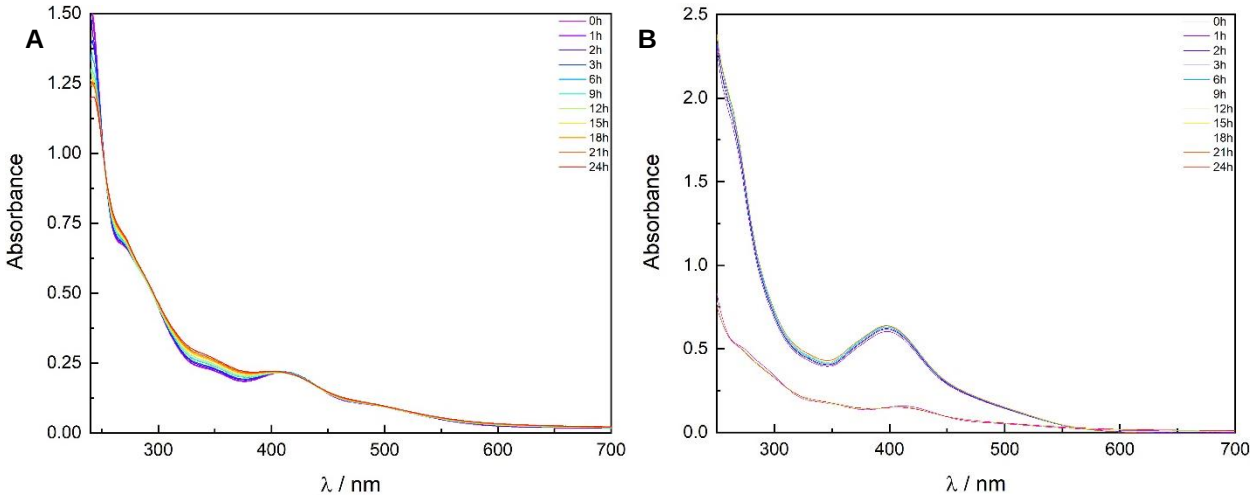

Fig. S52 UV Vis spectra of complexes **S1** (**A**) and **S2** (**B**) recorded over 24 h in PBS at 25 °C.

MTT assay

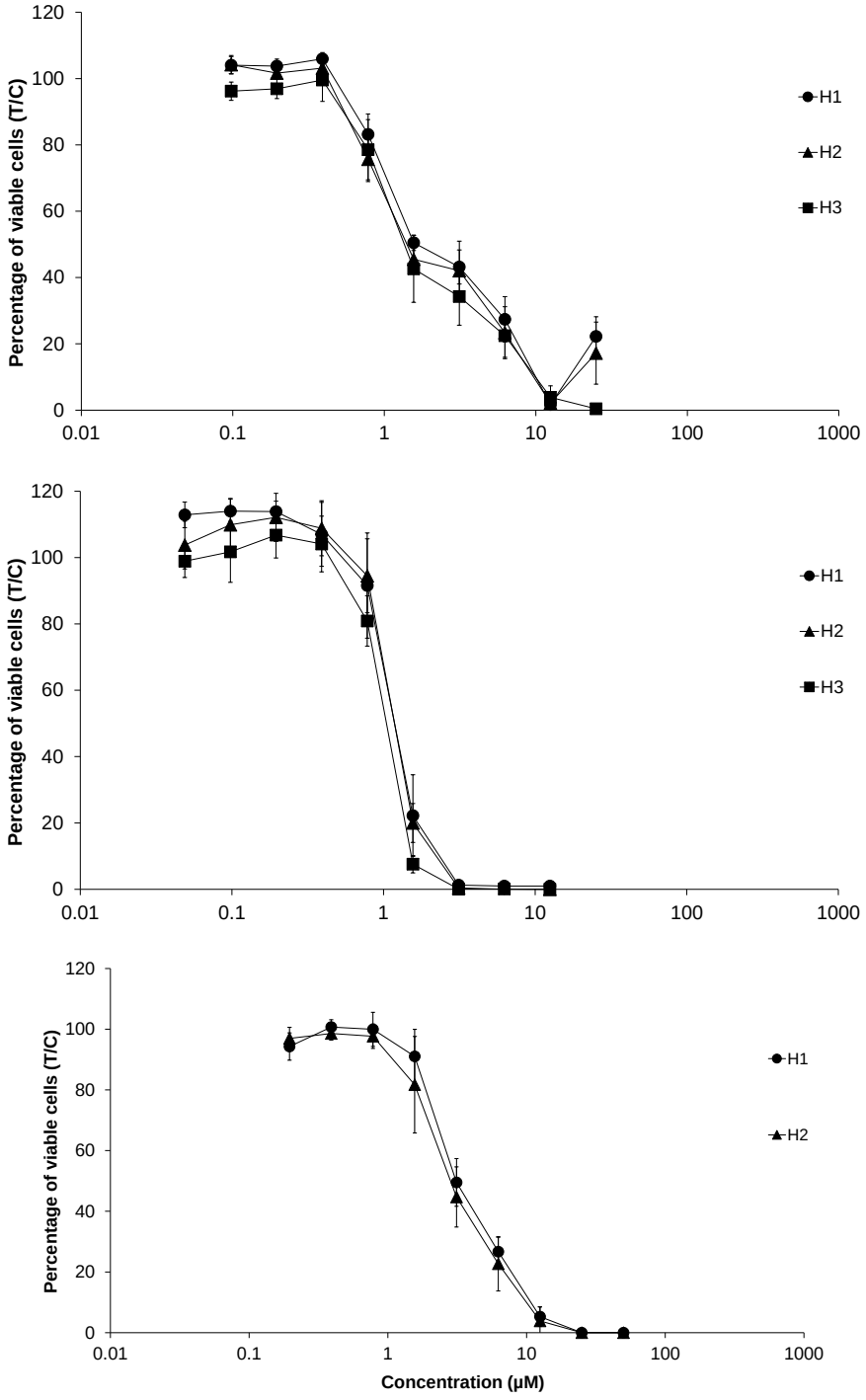

Fig. S53 Concentration-effect curves of compounds **H1**–**H3** in monolayer cultures of the human cancer cell lines A549 (top), CH1/PA-1 (center) and SW480 (bottom), as obtained by 96-h MTT assays (as far as active and reproducible).

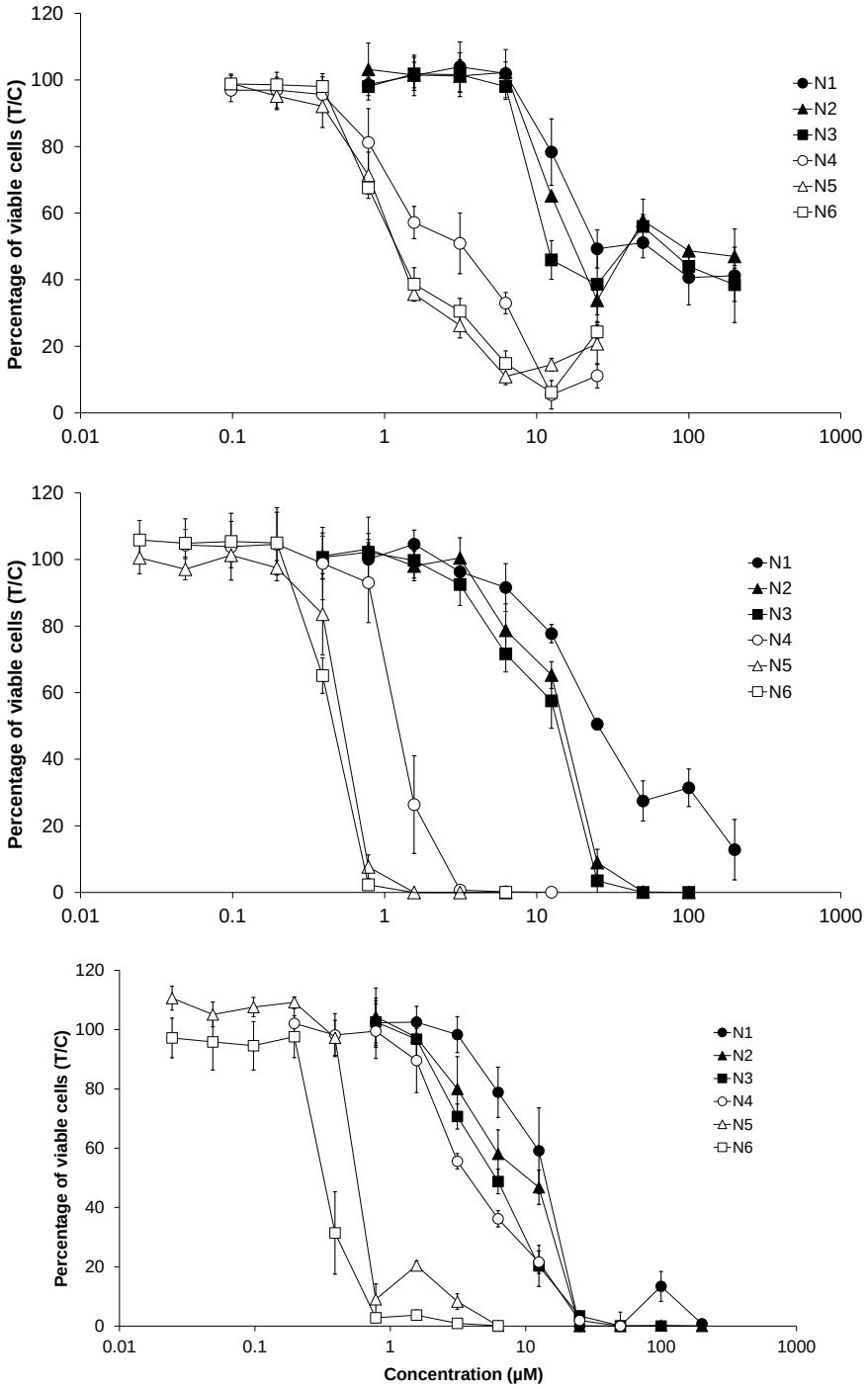

Fig. S54. Concentration-effect curves of compounds **N1**–**N6** in monolayer cultures of the human cancer cell lines A549 (top), CH1/PA-1 (center) and SW480 (bottom), as obtained by 96-h MTT assays.

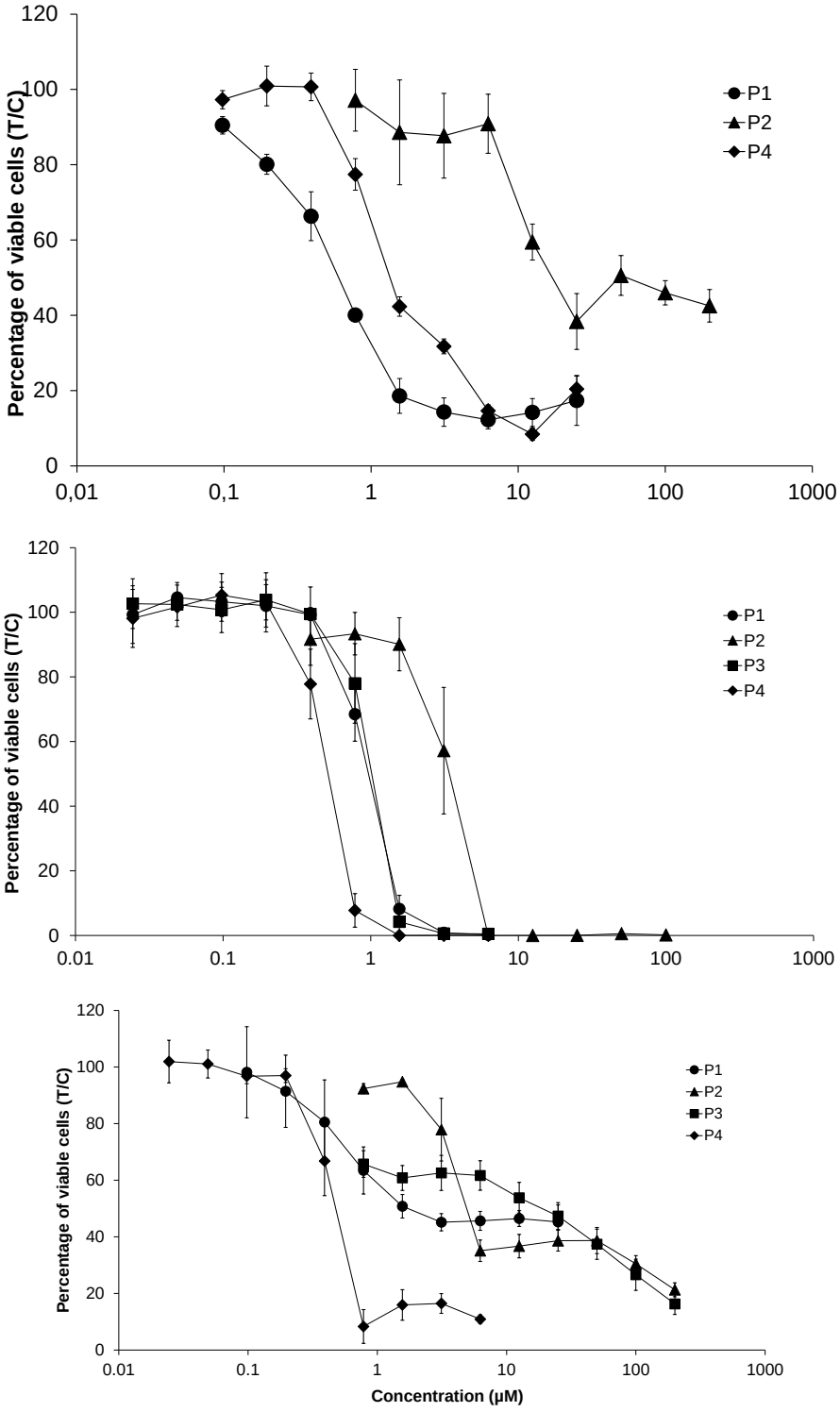

Fig. S55. Concentration-effect curves of compounds **P1**–**P4** in monolayer cultures of the human cancer cell lines A549 (top), CH1/PA-1 (center) and SW480 (bottom), as obtained by 96-h MTT assays (as far as active and reproducible).

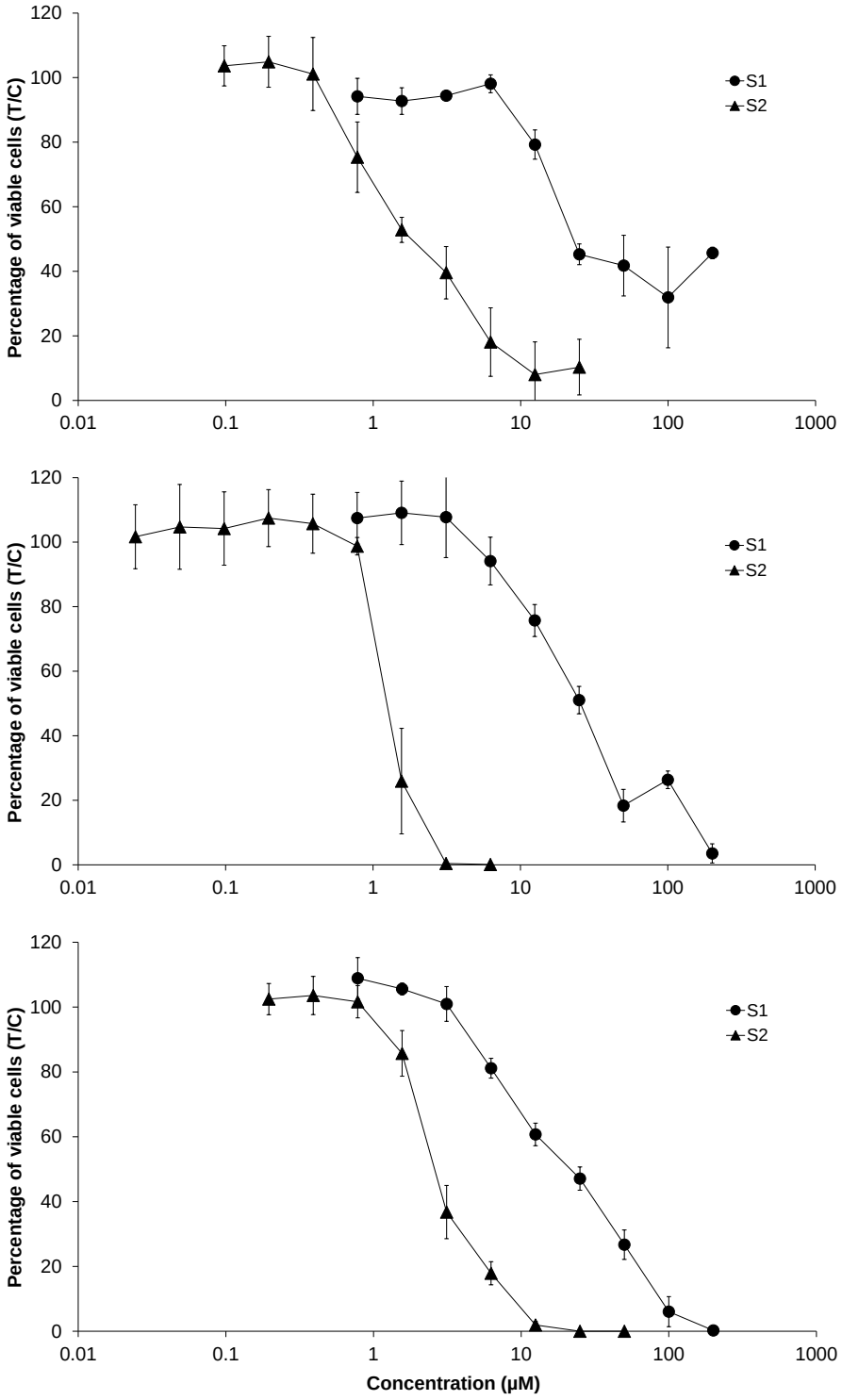

Fig. S56. Concentration-effect curves of compounds **S1** and **S2** in monolayer cultures of the human cancer cell lines A549 (top), CH1/PA-1 (center) and SW480 (bottom), as obtained by 96-h MTT assays (as far as active and reproducible).

Spheroid assay

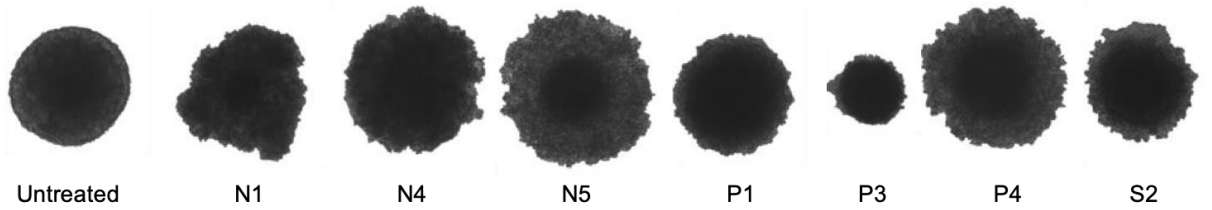

Fig. S 57. Representative images of CH-1 spheroids treated at the IC_{50} concentrations of the respective complexes for 96h.

Apoptosis assays

Flow cytometry assay

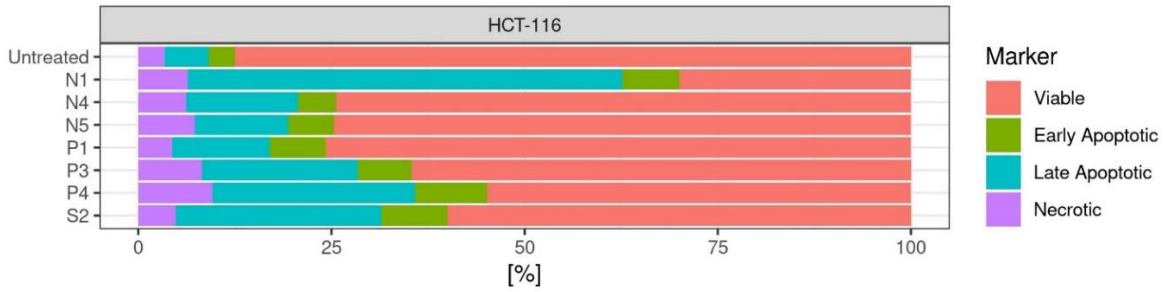

Fig. S58 Apoptose Graph depicting the percentual apoptotic stages of HTC-116 cells after treatment for 48 h with the respective compounds at 50% inhibitory concentrations.

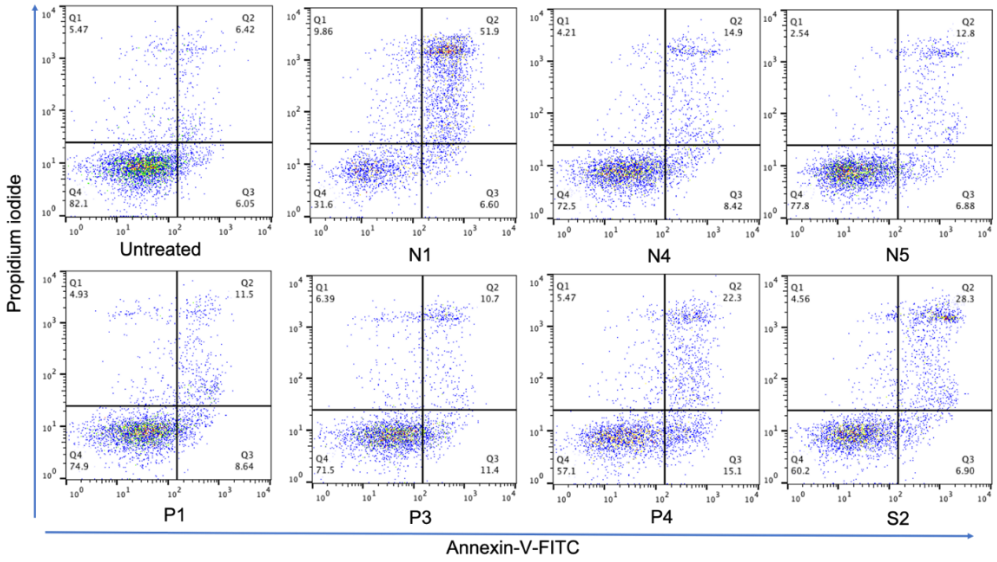

Fig. S 59 Representative dot plots showing the staining with annexin-V and propidium iodide on HCT-116 spheroids treated with the test compounds at IC_{50} concentrations for 48h.

Confocal microscopy assay

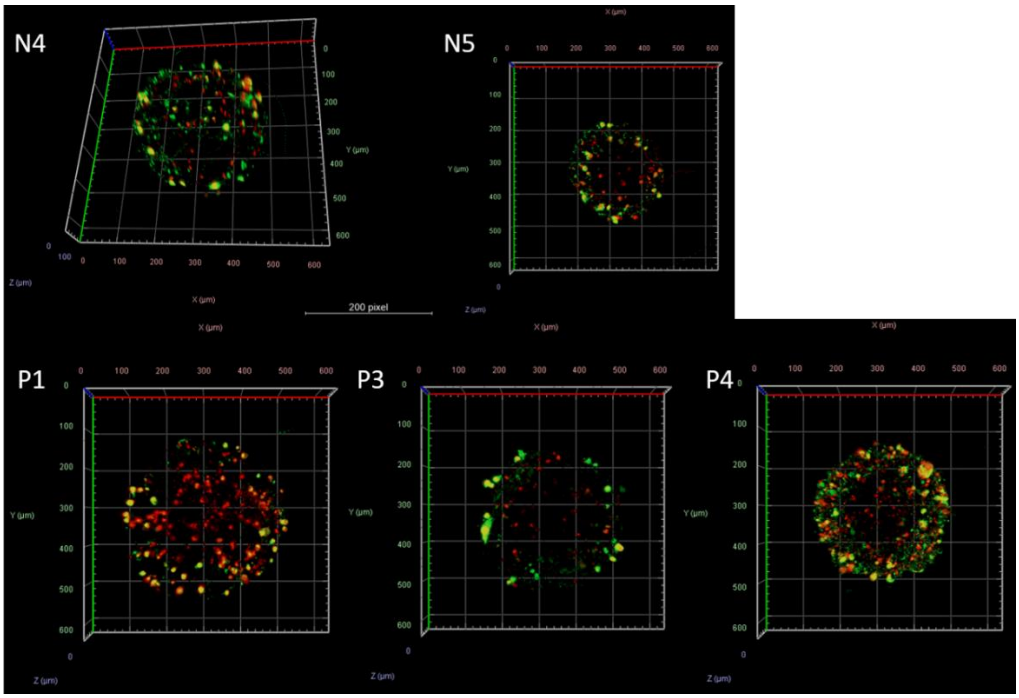

Fig. S60 Representative 3D reconstructions of HCT-116 spheroids (double-labelled with annexin-V-FITC and propidium iodide, abcam kit #14085) of untreated and treated with complexes **N4**, **N5**, **P1**, **P3**, and **P4** at their respective IC_{50} concentrations after 48 h. Confocal microscope images were obtained from a stack of optical sections.

Colonogenic assay

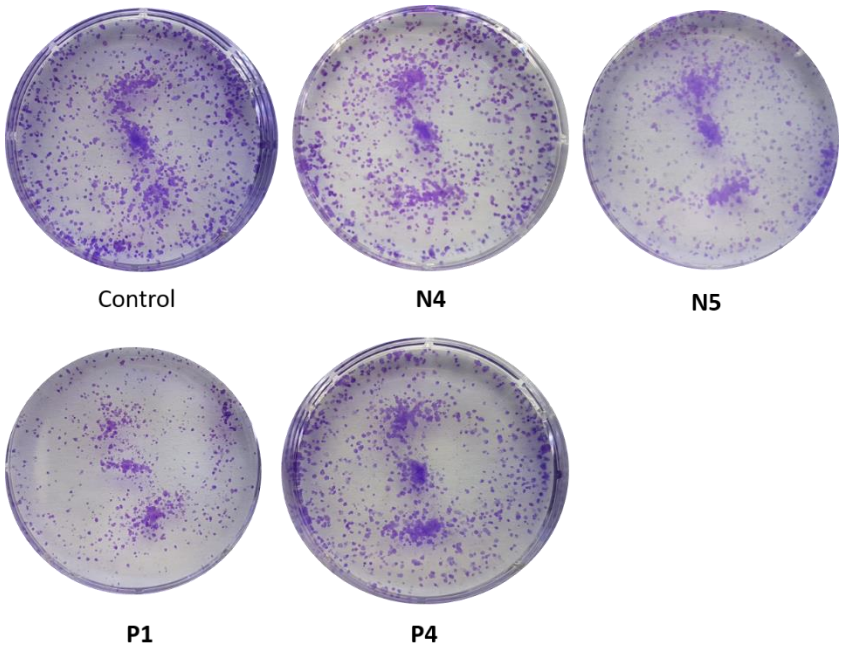

Fig. S61 Colony formation after 7 days of treatment with compounds **N4**, **N5**, **P1**, and **P4** in SW480 cells. Cells were treated at IC_{50} concentrations.

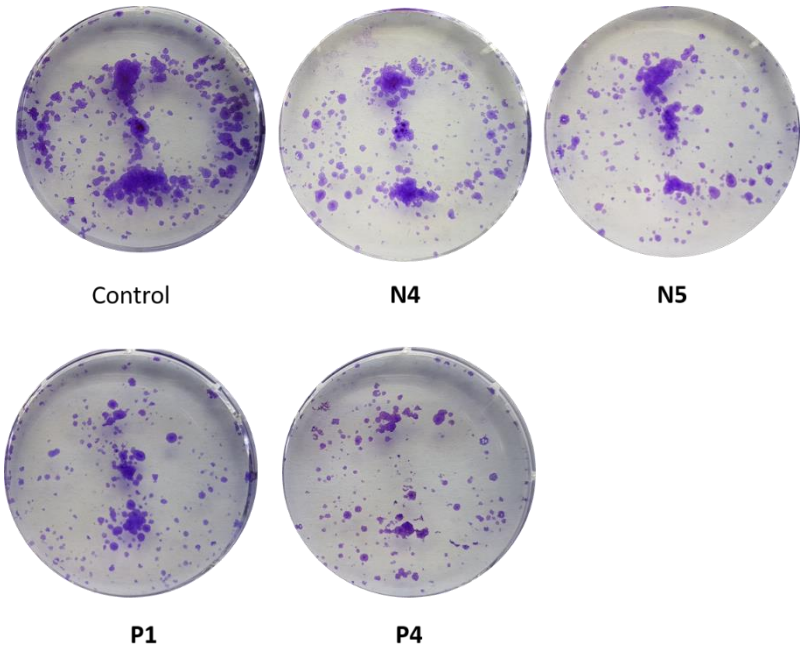

Fig. S62 Colony formation after 7 days of treatment with compounds **N4**, **N5**, **P1**, and **P4** in CH1/PA-1 cells. Cells were treated at IC_{50} concentrations.

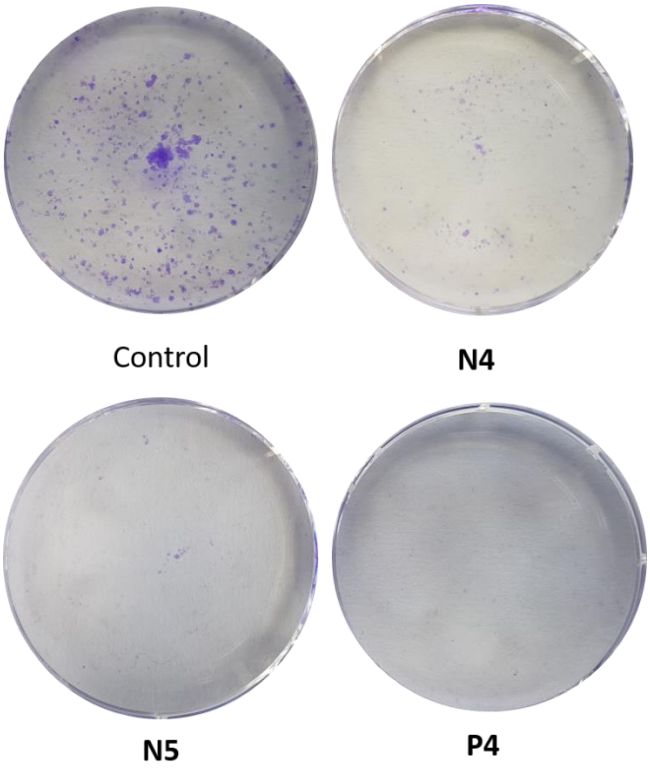

Fig. S63 Colony formation after 7 days of treatment with compounds **N4**, **N5**, and **P4** in A549 cells. Cells were treated at IC_{50} concentrations.

Plasmid assay results

Bar graphs

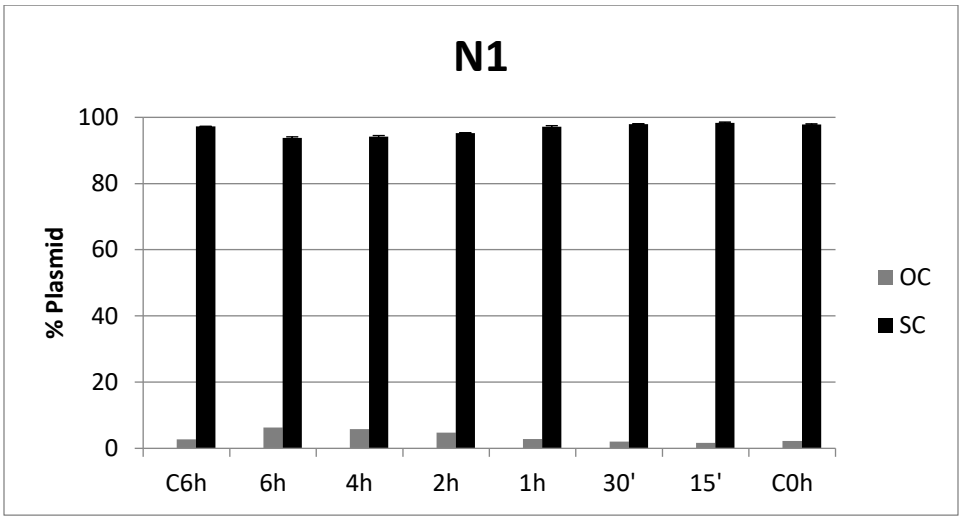

Fig. S64 Graph showing the ratio between OC and SC DNA strands of the pUC19 ds DNA plasmid after up to 6 h of treatment with compound **N1** at the respective IC_{50} inhibitory concentration. DNA strands after different periods of incubation at 37 °C with compound **N1** at 50 mM in the cell-free plasmid assay.

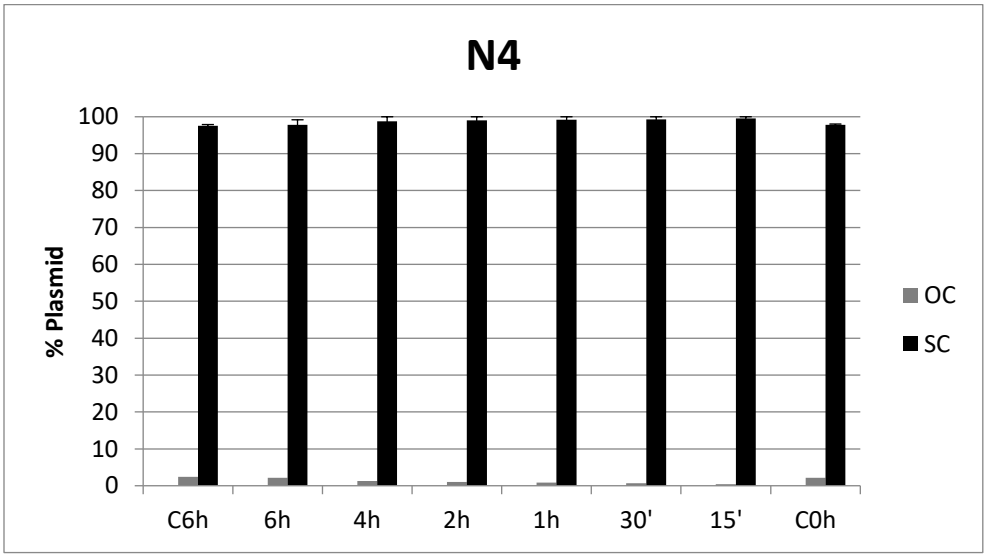

Fig. S65 Graph showing the ratio between OC and SC DNA strands of the pUC19 ds DNA plasmid after up to 6 h of treatment with compound **N4** at the respective IC_{50} inhibitory concentration. DNA strands after different periods of incubation at 37 °C with compound **N4** at 50 mM in the cell-free plasmid assay.

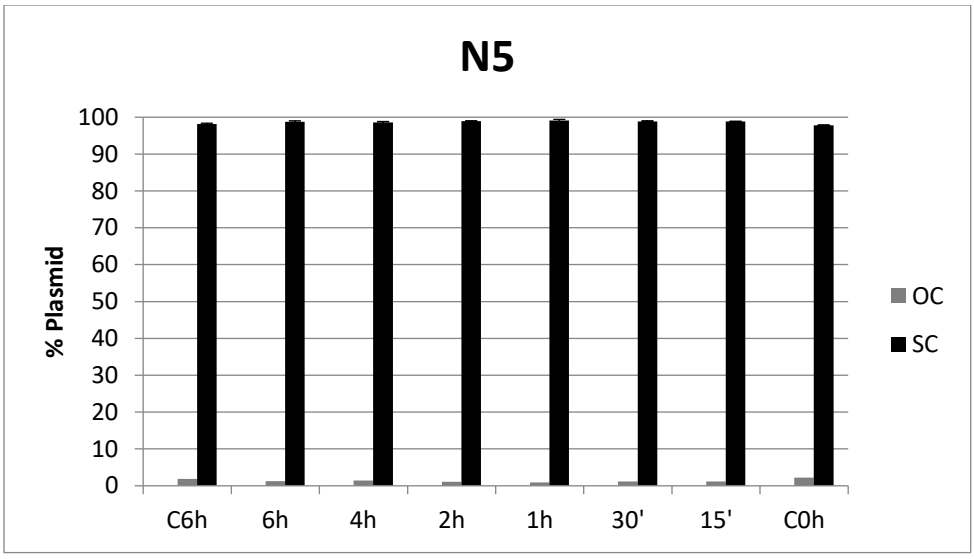

Fig. S66 Graph showing the ratio between OC and SC DNA strands of the pUC19 ds DNA plasmid after up to 6 h of treatment with compound **N5** at the respective IC_{50} inhibitory concentration. DNA strands after different periods of incubation at 37°C with compound **N5** at 50 mM in the cell-free plasmid assay.

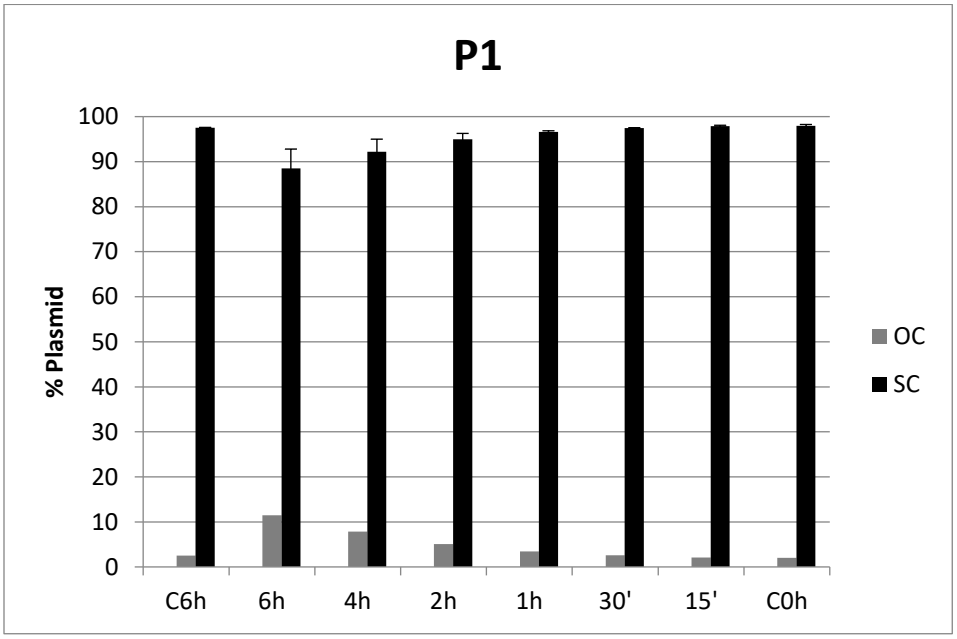

Fig. S67 Graph showing the ratio between OC and SC DNA strands of the pUC19 ds DNA plasmid after up to 6 h of treatment with compound **P1** at the respective IC_{50} inhibitory concentration. DNA strands after different periods of incubation at 37 °C with compound **P1** at 50 mM in the cell-free plasmid assay.

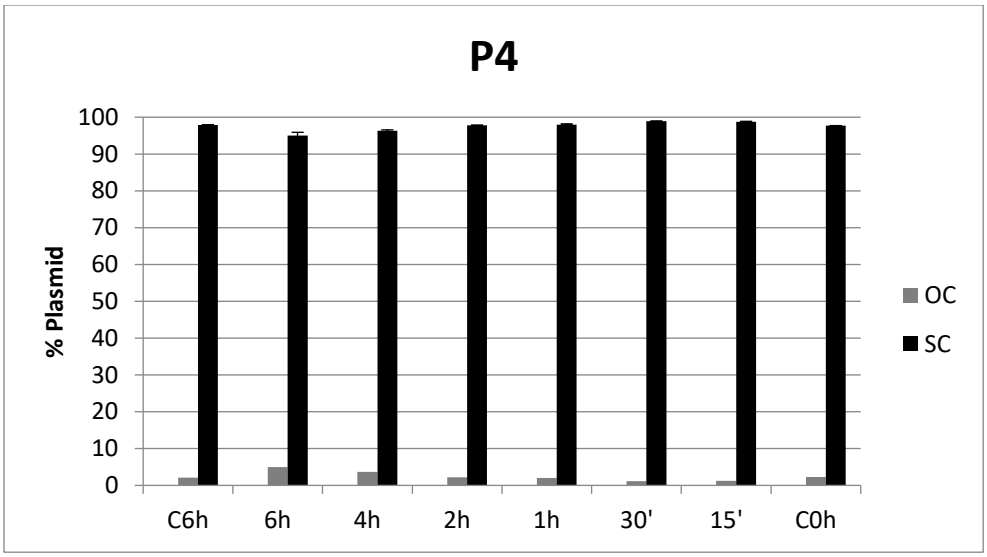

Fig. S68 Graph showing the ratio between OC and SC DNA strands of the pUC19 ds DNA plasmid after up to 6 h of treatment with compound **P4** at the respective IC_{50} inhibitory concentration. DNA strands after different periods of incubation at 37 °C with compound **P4** at 50 mM in the cell-free plasmid assay.

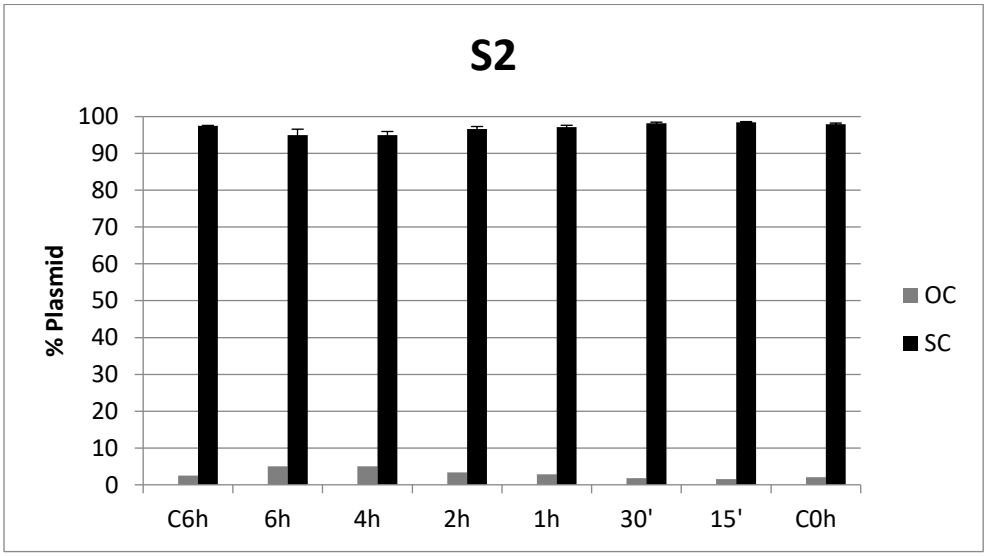

Fig. S69 Graph showing the ratio between OC and SC DNA strands of the pUC19 ds DNA plasmid after up to 6 h of treatment with compound **S2** at the respective IC_{50} inhibitory concentration. DNA strands after different periods of incubation at 37 °C with compound **S2** at 50 mM in the cell-free plasmid assay.

Agarose gel pictures

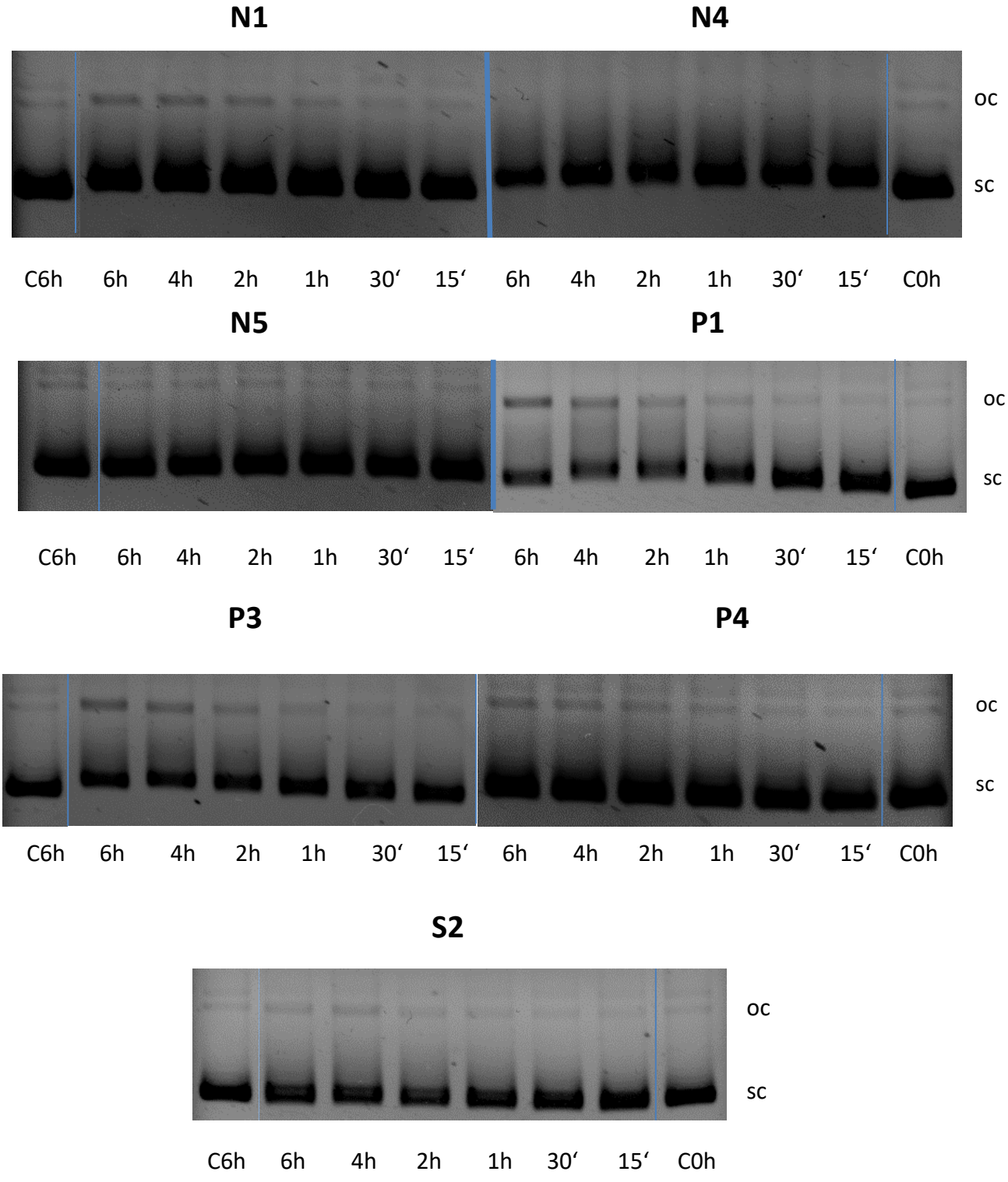

Fig. S 70 Representative pictures of agarose gels depicting plasmid(pUC19)-DNA-transformation upon drug treatment from 15 min up to 6 hours. ‘C0h’ and ‘C6h’ correspond to the untreated control sample at the beginning and end of the experiment.

Laser ablation ICP-MS

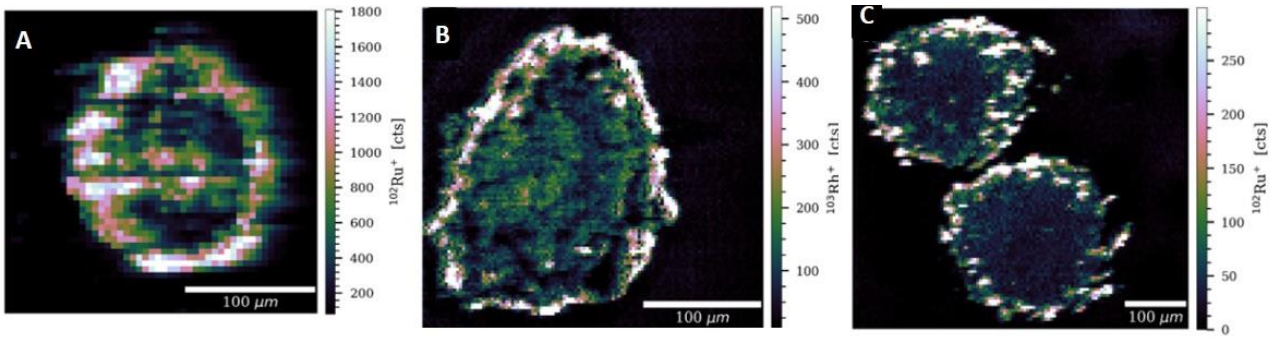

Fig. S71 Signal intensity maps of $^{102}Ru^+$ and ^{103}Rh obtained by LA-ICPMS analysis of HCT-116 tumor spheroids after treatment with **N1** (**A**), **N5** (**B**), and **S2** (**C**). High resolution LA-ICPMS images were obtained with a pixel size of 5 µm; scale bar 100 µm.